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BRAIN

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THE ADVANCEMENT OF LEARNING

BRAIN.

PART I., 1902.

Original Articles and Clinical Cases.

ON CONCUSSION OF THE BRAIN IN SOME OF ITS SURGICAL ASPECTS.

BY HERBERT W. PAGE, M.C., F.R.C.S.

Presidential Address.

In obedience to the custom which has prevailed here that the new President shall introduce himself to the Society by giving an address, and shall render at the same time his acknowledgments for the signal honour which has just been conferred upon him, I invite you to enter with me for a few moments on the consideration of concussion of the brain in some of its surgical aspects. Availing myself of Presidential, if not exactly poetical license, I shall use the term concussion of the brain in the widest sense, to include much that accompanies, and is a good deal more than simple concussion alone. The subject is well worn, but not believe, by any means exhausted, and there are su members in any section of this learned society can ever fail to be of interest, and sometimes o concern. In the first place to the surgeon, bec exercise of his skill, both diagnostic and manual, from concussion may perchance find relief or impending death; to the physician whose p to interpret some of the later consequences of intra-cranial injury when the immediate effects of accident have long since passed away; to the physiologist, because of the many transient or lasting derangements of function in all parts of the body to which concussion may give rise; to the psychologist, because of the subtle derangements of intellect which may seem to have had their beginnings in sudden physical commotion of the brain, and to all alike, singly or in company, by reason of the problems which concussion may present for solution at the bedside.

In the course of my hospital career I have had before me, like every other surgeon, a large number of cases of head-injury, and in the presence of no one of them have I not been conscious of the intricate difficulty of the problems to be solved, or very frequently not been eager to discover some ground, however small, for bringing relief and it may be rescue from impending danger to the injured person. The conditions of modern surgery, anti- or a-septic, as the practice of the individual may decide, come here to the surgeon's aid, and that which has been found practicable in the case of other closed cavities and serous membranes, and the diseases confined by them is, we all know, equally practicable in the case of the skull and the membranes of the brain. I compare the state of things now with the state of things in my student days. Then, hesitation in resorting to surgical measures, even by the least fearless surgeons; now, the fullest confidence that the chief danger of wounds has been removed. Then, the unhappy prospect, too often fulfilled, of meningitis, pyæmia, and death; now, the practical certainty that not one of these dire consequences is to be feared. During the last fifteen years of my practice at St. Mary's Hospital I find that in only two cases of head-injury, [illegible] of which was subjected to operation, was death [illegible] about by visible septic agencies: one from septic [illegible], the origin of which was never explained; the [illegible] ase of a fracture through the middle fossa having [illegible] mmunication between the cranial cavity and the [illegible] which was affected with chronic suppuration. [illegible] bt that the experience of other surgeons has been like my own, or that I shall not meet with general agreement when I say that it is not sepsis which is most to be feared in connection with injuries to the cranium and its contents.

I venture, therefore, to take up the position that surgery may be even bolder than it has hitherto been in endeavouring to minimise and remove some of the causes which seem to lie at the root of many of the later consequences of severe head-injury, in cases where accurate diagnosis may be impossible and the surgeon has to rest content with speaking of them as concussion of the brain, uncertain as to the precise injury which has been inflicted.

The more obvious grounds for surgical interference are of course well recognised. Few, I might say none, would now hesitate to elevate depressed bone and remove all fragments which have been driven into the brain substance. The indications are sufficiently clear when there is a scalp wound, but it has never to be forgotten that injury to bone and the deeper table of the vault of the skull may be more extensive than outside appearances suggest; and furthermore, that the existence of depression may be told only by some sign of cerebral disturbance. A case of the kind fell to my notice some years ago in which a small scalp wound in the occipital region with an insignificant fissure of bone beneath was followed in a few days by rise of temperature which could not be accounted for by anything visibly untoward at the site of the injury. The high temperature was, however, regarded as a warrant for exploration, and it was then found that the inner table had been extensively broken up and depressed. Elevation and removal of bone fragments were forthwith followed by normal temperature, and the course of the case was thereafter without incident. I thought at the time that the rise of temperature was in all probability due to disturbance of the thermotaxic nervous mechanism, and the absence of all sign of septic mischief, either in scalp, bone, or membranes, seemed to justify that conclusion.

And here I may interpolate the observation that wounds of the scalp with even extensive local injury to the bone and more vital parts beneath do not provide by any means the worst varieties of head injury. Let me recall for example the following cases of severe local injury with which I have had to deal: (1) A large portion of the squamous part of the temporal bone driven in by a blow from the shaft of a gig, with extensive laceration of the temporo-sphenoidal lobe and considerable hæmorrhage at the base; (2) Extensive pond depression of the parietal bone with much laceration of membranes and brain, the result of a fall from a height; and (3) a like injury from a blow in the occipital region with many particles of bricks and mortar driven into the substance of the brain and followed by temporary hemianopsia These were all cases in which the severity of the injuries to bone, membranes and brain substance seemed to offer neither let nor hindrance to the progress towards recovery, and I am inclined to believe that traumatic opening of the cranium may be an element of provisional safety and materially lessen the tendency to death. At any rate, if it be true that increase of intracranial pressure is one of the chief sources of danger after so-called concussion of the brain, be the actual cause what it may, the fact that provision for the escape of blood has been made by an opening in the skull must surely lessen if not altogether annihilate this particular danger. I feel pretty confident that in some cases in which there has been the necessity for surgical interference and the amount of bone to be replaced or removed has been insignificant, the chief benefit has accrued from the escape of blood which must otherwise have exerted injurious pressure on the brain. This was well exemplified in the case of a lad who had been struck on the side of the head by the buffer of an engine, and for whom it was thought right to turn down a flap of scalp in order to examine the bone beneath. A longitudinal fissure fracture running from back to front an inch above the auricle and a vertical fracture extending thence into the base were found, and from these lines of fracture there poured such quantities of blood that it was deemed useless to make further exploration through the bone. Improvement, however, soon set in, and although a long time elapsed before brain function was entirely restored, I had little doubt that compression was prevented by the outflow of blood and that to this fact the happy issue of the case was mainly due.

Another very obvious ground for surgical intervention lies in compression of the brain from meningeal hæmorrhage, the most striking examples being those in which blood has been poured out from a torn artery, causing in the case of the middle meningeal those classical symptoms to which it is not necessary to refer. The difficulty which here confronts us is twofold. There is the uncertainty whether the coma of compression has really supervened upon the unconsciousness of concussion, more especially when there has been no "lucid interval" to tell us why there has been a change in the scene; and there is the further difficulty that symptoms akin to, and closely simulating, those which have been spoken of as classical may be attributable to lesions other than local meningeal hæmorrhage. More than once have I been disappointed when operating in the hope, though hardly in the belief, that meningeal clot would be discovered, and after death a totally different condition of things has been found, a condition of things which has taught no lesson for future guidance nor how to avoid such mistakes again.

In the same category lie those cases in which there has been laceration of one of the sinuses, lateral, longitudinal or other, from which the bleeding may be tremendous and may perhaps be revealed by rapidly formed swelling beneath the scalp when a fissure fracture has opened a channel for the escape of blood. Sinus hæmorrhage is not uncommonly revealed in this particular way, and surgeons well know the almost insuperable difficulties which arise in dealing with it. These then are the more manifest indications for early surgical intervention; and although experience tells us how often the character and extent of the lesions oppose a barrier to success, yet I think there is cause for thankfulness that not infrequently so much may be done.

Let me now turn for a few moments to the consideration of a different class of case in which operative interference might, I think, be more often resorted to, in the hope of averting some of the ill results of concussion of the brain.

And in order to a clear presentation of this part of the subject I must ask you to reflect very briefly on the kinds of symptoms which are not uncommon after concussion, and in the next place on the several lesions, cerebral and other, which we are wont to find on the *post-mortem* table. Putting on one side the state of unconsciousness which may be regarded as due to the shake of the whole brain mass, as defined by Hutchinson, rather than to any special lesion, the notes of cases tell of various symptoms, some of which are of definite value for purposes of localisation, while other symptoms are of no such value according to our present knowledge. Convulsions of the Jacksonian type, owning a definite onset and march, are not often seen as an immediate result of injury; more commonly, as all know, they are the remoter result of a circumscribed local lesion, depressed bone or extravasated blood for example, either of which may lead to thickening of membranes and cause pressure on the cortex and even invade it with inflammatory products. General clonic convulsions, however, are of not infrequent occurrence, and I have been surprised to find how often it is recorded in the notes of cases that the patient had a fit or succession of fits, two or three, without special localising value, within a few days of admission to hospital. I am content at this moment to note the fact and to wonder in passing what in such circumstances a fit or convulsion really is.

Severe persistent pain is, moreover, as everyone knows, a not uncommon symptom, and here I speak of pain of seemingly more special and serious import than that which the patient may describe as merely a bad headache, pain so intense it may be as to prevent sleep and to overcome that tendency to drowsiness which is often so striking that Hutchinson deems it worthy of providing a name for the second or "sleepy" stage of the several stages into which he divides the phenomena of brain concussion. Here again I am content to notify the fact and pass on, that I may speak of the high temperature which often supervenes after severe concussion. This was noticeable in a large proportion of the cases which ended fatally. The temperature rose before death to considerable heights, from 103° F. to 106° F., even when there was no suspicion of sepsis. And that which is seen so often in fatal cases is not uncommon, though much less frequent, in those which survive. I have already referred to a case in which such elevation of temperature was taken as an indication of the need for surgical intervention. At any rate the onset of high temperature is to be regarded of evil omen, and there can be little doubt that it is due to derangement of the apparatus for heat-adjustment in the brain, and may even be more than suggestive of the existence of cortical lesion.

Consider in the next place the kinds of lesions which are met with after concussion of the brain. Bruising of the cerebral tissue in varying degrees of depth and superficies beneath the seat of blow, and bruising in many instances at the opposite point of the cranial cavity, are seen every day, with hæmorrhages here and there; and we need not stay to inquire whether a better explanation thereof is to be found in the theory of vibration and *contre-coup*, or in that of cones of depression and bulging, with rush of suddenly displaced cerebrospinal fluid from the lateral ventricles through the Sylvian aqueduct and fourth ventricle, whereby the walls of the latter are violently torn. For such lesions there is, I fear, not much to be done, for the base of the brain where they chiefly fall is inaccessible; nor of course can surgery intervene on behalf of the punctiform hæmorrhages which dot the cerebral mass, even had the surgeon the means of knowing for certain that they were there. At all events it is questionable whether these minute extravasations are in themselves of serious moment: their number and diffusion are rather indicative of the violence of the commotion to which the brain has been exposed. It is otherwise, I take it, with extravasations of blood which are found in various parts and in various amounts on the surface of the brain. Thus there are hæmorrhages between the dura mater and the bone, commonly but not invariably owning some definable source, as from rupture of a meningeal vessel of anatomical dignity; hæmorrhages beneath the dura in the arachnoid or subarachnoid tissues and spaces, occupying the surface of the hemisphere, or collected in measurable quantities towards the base of the skull, and admittedly of very common occurrence indeed; and hæmorrhages of greater rarity in and beneath the pia mater itself, as depicted in one of Hutchinson's most beautiful illustrations. For these two last forms of hæmorrhage no source so definite is always to be found as can be found in the case of hæmorrhage between the dura and the bone, but it is conceivable that sometimes it may be due to smaller and weaker vessels having, according to the suggestion of Miles, lost the accustomed support of the cerebrospinal fluid which has been violently expelled from the cranial cavity. However this may be, they are hæmorrhages which I cannot help thinking may have a serious effect, both immediate and remote, on cerebral function, and I ask the question, ought not such extravasations of blood to be removed if possible? In the case of the rare pial hæmorrhages this is manifestly out of the question, but it is very different in the case of subdural extravasations. When the injury has made an opening through both skull and dura a way of escape for blood has been provided, and one at any rate of the reasons why lacerations of the brain in association with wound and depressed fracture are possibly amongst the least serious of head-injuries is herein to be found. I recall cases where the copious escape of blood has presumably been of much value in determining their favourable course, and when elevating bone and removing foreign particles or broken-down cerebral tissue I have considered the surgical measures incomplete until blood from the surface of the hemisphere or from the base of the skull had been washed out with a stream of water. The path of diagnosis is comparatively easy when the skull has been opened, and it is obvious what is the best thing to do, but it is otherwise when we have to try and solve mysterious and may-be insoluble indications with the cranium closed. What would not the surgeon sometimes give to know what has actually occurred? Speculation and conjecture from his dead-house experience are open to him, and in these I fear he must still very frequently indulge, for it is hardly probable that he will often adopt the plan of Tuffier, and practise lumbar puncture to discover whether there is blood-staining of the cerebrospinal fluid and presumptively fracture of skull with subarachnoid hæmorrhage. Even, however, if there are no precise indications forthcoming, the surgeon is surely justified in doing that which in another instance accident might have done for him—make a harmless opening in the skull, if haply thereby, in a matter of life and death, he may find or do something to turn the scale in favour of the one, rather than leave the unconscious and helpless sufferer before him inevitably to meet the other.

Is it, however, invariably the fact that there are no indications to suggest that the hæmorrhage of which I have been speaking exists? From the frequency with which it is found after death it is warrantable to conclude that it must be present also in many of the cases which survive, just as we are justified in a like conclusion with regard to the bruising of cerebral tissue and the punctiform hæmorrhages here and there throughout the hemispheres. Would the surgeon do wrong to act on such assumption only? I trow not; but if by chance there are any of the symptoms to which reference has been made, the convulsions, the muscular rigidity, the rise of temperature, the severe pain due to cortical irritation or pressure, not to mention duration of unconsciousness, then it seems to me there are real grounds for resorting to operation, that the offending extravasation of blood may be washed away or the offending cause removed. Most surgeons must have met with cases in which, after concussion of the brain, there have been indications of what is often termed cerebral irritation, varying from mere momentary twitching of muscles to more definite convulsive movements affecting the face and limbs. The question has been anxiously debated whether operation should or should not be resorted to, but the immediate course of the case has seemed to discountenance intervention, little thought being given at the moment to remoter issues, and when at length the dead-house has been reached, there has been deep regret that intervention had not been made. And there are other cases where, in such circumstances, intervention has been followed by the happiest results, as in one notable case, which I had the opportunity of watching, recorded by my colleague, Edmund Owen, who deemed it right to explore because of "cerebral irritation," shown by oft-repeated clonic convulsions, involving the forearm, fingers, and face, with some aphasia, which began on the fifth day after a fall on the head—a case at first of apparently simple concussion in a child—restored quiescence by washing out subdural blood, and repeated the process on return of the symptoms with final and complete success.

Reference also may here be made to the remarkable case of Mr. Raymond Johnson and Dr. Risien Russell, recorded in the last volume of the *Transactions of the Clinical Society*, a case of traumatic subdural hæmorrhage occasioning convulsions on the sixth day after the injury, and successfully treated by operation A man was found at the bottom of a flight of stone steps with a scalp wound on the left side of the head, and under the combined effect in all probability of sleep, concussion and alcohol, lay unconscious for some hours. For five days there were no particular symptoms, and then he had a fit, and fits were frequently repeated until on the sixth day he came under their care. There was much variation in the character of the convulsions, but many began by twitching of the left side of the face, and others by movements of the left hand, facts which, in association with weakness of the left arm, exaggeration of the left knee-jerk and extensor response on the same side, were regarded as indicating the existence of definite irritation of the right hemisphere. The evidence was insufficient to justify the diagnosis of a focal lesion, for the onset of the fits was variable, and the other phenomena could be as well accounted for by a general disturbance of the right hemisphere. But although there was the long interval of six days between the accident and the onset of convulsions, and there was a possibility that after all the case might have been mistaken for one of idiopathic epilepsy, it was resolved to explore over the middle of the right Rolandic area. Some three drachms of blood escaped from beneath the dura, and the wound was closed. There was no return of fits, and although convalescence was somewhat delayed by an attack of delirium tremens and other complications, the ultimate restoration to health was assured. It is interesting to note how considerable in both these cases was the interval between the receipt of injury and the onset of the symptoms whereby the surface hæmorrhage was revealed.

Worthy it seems to me of a place in the same category is a case of my own, although the indications of intracranial mischief were neither so striking nor so urgent in their onset and course. A man, age 25, was admitted under my care in St. Mary's Hospital, in November last, with a history that twelve weeks previously he had been kicked by a horse on the top of his head. There was no wound. He was unconscious for twelve hours, but after a week's rest at home he resumed his work. He was obliged, however, to leave it because of attacks of transient giddiness, together with persistent pain at the site of the blow. Thus complaining he was sent to St. Mary's, and in addition there was distinct tenderness over the part where he had been kicked. One spot, an inch from the middle line and one inch in front of the right Rolandic fissure, was especially sensitive. He was, moreover, morose, reserved, and apathetic, and gave one the impression of suffering in the way he described. There was no improvement from rest in bed, and his head having been shaved, a decided flattening of the skull, not amounting to circumscribed depression, could be both seen and felt at the place where he had been struck. Those were the sole indications of cranial or intracranial disease, but they were sufficient, I thought, to warrant exploration, and accordingly on November 22, after having had him under observation for a fortnight, I opened his skull at the point named, in the expectation that at any rate some depression would be found from splintering of the vitreous table. There was really nothing to be seen wrong with the bone, but the dura mater was unduly adherent, it protruded rather more than usual, and no pulsation was to be felt. I therefore incised it, and arachnoid tissue protruded in such a manner as to suggest that pressure had been relieved. The protrusion looked so like a thin cyst-wall that I cut into it; a small quantity of blood-stained fluid escaped, and a probe could be passed into a distinct cavity between convolutions. And now pulsation became evident. Content with what had been done, and believing that enough to account for his symptoms had been found, I closed the wound. Progress since has been favourable without interruption; the pain has absolutely gone, the man is bright and cheerful, he no longer has attacks of giddiness. He believes that he has been completely cured, and save for the reservation that attaches to all such operations, I hope that we may believe it also, not only as regards his present, but as regards his future likewise. It is not too much, I trust, to assume that a timely operation has rescued him from far graver evils, from fits, from paralysis and melancholia, from serious cortical degeneration. And if this is really so, I am not concerned to ask how trivial may have been the basis upon which the trephine was used. I need not labour the point any more, but will be content to express my conviction that the surgeon will often do well to intervene, even when there is no certain indication of definite focal lesion, that he may rid the cortex of the brain from the presence of extravasated blood, which if not now, may nevertheless in the future do incalculable mischief, rather than leave the injured person to his fate. The operation ought to do no harm; on the contrary, it may be followed by lasting good.

There is, however, yet another aspect from which the question of operative interference may be viewed. No one will deny that various kinds of mental disorder are fairly common after concussion of the brain. In my own limited experience, and out of the comparatively small number of cases which have passed through my wards, not a few have shown signs of mental aberration, not the mere transient clouding and confusion in the days immediately after the injury, but mental derangement of a more lasting kind. In medical literature there is no lack of instances of unquestionable traumatic insanity, and the views of many writers are to be found therein. To name one or two only. Crichton-Browne has written that "a careful inquiry will establish the principle that cranial injuries are, at least, prolific sources of mental derangement," and that "concussion is . . . the more important element in the vast majority of cranial injuries in relation to subsequent mental incapacity" and "the most fruitful source of ulterior misfortune."

Kraft-Ebing, too, in his well-known monograph, has dealt very fully with this aspect of concussion of the brain, and has shown that severe headache, diffuse or local, is a common premonitory sign of mischief, and that while there are no constant pathological changes, a "diffuse chronic peri-encephalo-meningitis" is most frequently to be found, together with local cranial lesions and adhesions of the dura to the bone. The same conclusions are reached by Dr. Powell in his masterly thesis (1893) on "The Surgical Aspect of Traumatic Insanity," wherein is collected a series of 67 cases of combined traumatic insanity and epilepsy, a large proportion of which were permanently benefited by operation. It is true that Clouston with his unrivalled experience is of opinion that "accidents to the head do not loom largely in the production of the insanity of the world"; but, while recognising his high authority, and granting that the natural tendency on the part of relatives to regard injury rather than inheritance or disease as the cause of insanity detracts from the value of statistical evidence, the record of published cases is sufficiently striking to arrest attention, even though our own experience did not infallibly tend in the same direction. How often, indeed, have we not heard that the onset of "fits," using the term in the widest sense, has followed some injury to the head, that changes in disposition and temperament, incapacity for sustained mental occupation, inability to engage in the former pursuits, liability to suffer from severe headaches, persistent sleeplessness, loss of memory, attacks of depression and melancholy, moral deterioration, and other kindred steps in nervous dissolution have seemed to have had their beginnings and to date their onset from some head-injury spoken of at the time perhaps as slight concussion of the brain? We are hardly in the position yet to attribute the various mental phenomena to definite focal lesions, to say, for example, that change of temper is always due to injury of the frontal lobes, much though there is in support of this view, or melancholia to lesion of the parietal, but is it not possible, nevertheless, that many of the conditions which have been named may own a material cause in cortical degeneration, started not by gross lesions like depressed bone and torn membranes and bruised cerebral tissue, but in surface hæmorrhages which are comparatively harmless at the time of their effusion? Were one without clinical experience to be shown two cases side by side, the one an example of compound depressed fracture with lacerated membranes and fragments of bone driven into the cerebral tissue—circumscribed local lesions every one—and the other an example of surface hæmorrhage with cranium intact and membranes whole, nothing more he might remark than a little blood, and were asked to compare the prognostic importance of the several lesions, who can doubt which would appear to him the more serious? I think he might be wrong, for the seemingly lesser lesion may after all be the more serious if the blood be not entirely removed and its continued presence come in time to arouse inflammatory changes and adhesions whereby the cortical superficies may be affected and evil consequences ensue.

Let me relate a case in point. A man, aged 30, who had not had syphilis, came under my care in March, 1897, with a history of having been stunned by a fall from a cart on the right temporal region in 1889, eight years before. Nothing was thought of the injury at the time and he resumed his work, but in four days he had a "fit," and was unconscious for ten minutes. Soon afterwards he had another, and then fits recurred at intervals of two or three months, becoming recently more frequent. Their nature was indefinite, without constant onset or march, but nevertheless suggested the propriety of exploring over the right Rolandic area. No focal lesion was discovered. There was temporary improvement, but nothing more, and he steadily degenerated into epileptic dementia until the morning of January 31, 1901, when he was found unconscious in bed. He was brought to the hospital and died comatose on February 4. At the necropsy the skull was found of variable thickness, and on the anterior surface of the right petrous bone, extending forwards to the squamous portion, was a raised patch of bone with a defined edge, looking as if it had been the result of periostitis. Several bony spicules projected inwards from the temporal and occipital bones, and although after so long lapse of time there could be no actual certainty, the general impression was that there had been a fracture of the base in the middle and posterior fossæ. The dura mater was adherent to the bone in several parts of the vertex, and there were signs of old lepto-meningitis anterior to the Rolandic areæ. The membranes were adherent to the brain, and the two hemispheres were firmly adherent to each other for quite half their long diameter.

This is, I think, a notable case in all its features, and one can hardly evade the question, could surgery have done aught to prevent the deplorable consequences of the head-injury which this man sustained, and which, with a never-ceasing train of symptoms, and after much suffering, eventually brought about his death? Putting aside the cranial lesion, for which there was no remedy, but which clearly did not cause his death, there yet remains the probability that surface hæmorrhage was abundant, and that had this only been removed the widespread lepto-meningitis and resultant cortical changes might have been prevented. I admit the probability only, and that there may have been no symptoms to warrant early exploration, even though in four days he had a "fit," and I must admit also how little so far in such circumstances surgery has been able to accomplish.

A striking answer to the question which I have this moment put may be found in the brilliant success obtained in a case which shall be the last with which I will trouble you; a case of basal fracture recently recorded by Poirier, who in describing it complains that modern surgery has done so little for such injuries, and who advocates, as I venture to advocate, more active treatment than mere disinfection of the ear, pharynx and nose. A man, aged 32, fell from a ladder and sustained, as was believed, a basal fracture in the anterior fossa, bleeding from the nose and subconjunctival hæmorrhage supporting this diagnosis, his temperature having in the course of six days risen to 39 8° C. and his pulse having fallen at the same time to 60, with headache and slight delirium, but no paralysis. The skull was opened in two places with chisel and mallet above each ear. The tense unyielding dura was incised and a considerable quantity of sticky, blood-stained fluid was evacuated. Raising the temporal lobes with the finger gave exit to the same kind of fluid, and drains were inserted beneath the temporal and sphenoidal lobes as far as the tentorium. The temperature fell the same evening and the pulse-rate rose. This improvement continued, and in thirty-six days the patient was discharged well. Lumbar puncture had been resorted to before the operation, and from the fluid withdrawn cultures were made of the staphylococcus albus and aureus, confirmatory of the view held by Poirier, that meningitis had been set up by septic invasion from the nasal cavity.

This remarkable case is more encouraging than my own experience, but not my hopes, would seem to warrant, for from the point of view of operative interference I have made a careful examination of all my cases which have ended fatally, and with one or two doubtful exceptions it has been only too clear that operation could have been of no avail to save life. And so must it ever be, I fear, with all cases of the kind where, from the nature of the injuries, whether to bone or brain, the issue is never in doubt; but there is left to us the larger number of those who survive and of whom some, at least, may present signs of intracranial mischief for the rest of their lives. It can hardly be questioned that in order to be successful in its object surgical intervention must be made early, rather than when symptoms have arisen to tell that mischief has been already done. In the timorous days of pre-antiseptic surgery not a few surgeons used to put off the elevation of depressed bone until there were other indications for operation; used to wait, in fact, until some further harm had been done. It is not less imperative to be reminded that in the case of symptoms dependent on chronic inflammatory changes their prevention is better than their cure. When the habit of "fits" has become established, the scope of successful surgery is seriously diminished.

Of the technique of surgical methods there is nothing that need be said, but I would advocate the more general custom of shaving the head, without which a proper examination of the skull is almost impossible. Indeed it is not necessary for me to enter into surgical details, for no surgeon of experience will be at a loss how to meet the difficulties which may confront him; his chief, his only, difficulty may be to know when he may justifiably intervene. To this end he must surely be more than a mere chirurgeon, a worker with the hands; he must, while not forgetting the revelations of the *post-mortem* room, combine in his person, if he can, something of the physician, something of the physiologist, and something also of the psychologist, if he is to be fitly equipped for the work in hand. The combination may further be of advantage to himself and others if it saves him from yielding to the temptation to operate for the simple love of operating and leads him to cultivate the art of diagnosis upon which the success of his practice must depend. Thus only will surgery in the long run be well repaid, even though the actual number of successes may be few.

Here I must end and throw myself on your kindness to overlook the shortcomings and deficiencies—for they are many—of this address. That I shall not appeal to you in vain I know already, for by your generosity, not by my own deserts, it is that I find myself in this honourable place. And yet I must confess that somewhere in me, surgeon though I am, there is a substratum of genuine love for neurological work and real interest in the advancement of the science and practice of neurology. I fully believe that this is largely due to my having come at the outset of my career under the splendid influence of the first illustrious President of the Society. My days as a student at the London Hospital were passed in the awakening dawn of a new era in neurology, for Hughlings-Jackson was at the time engaged in the earliest of his clinical observations, whereby with the insight of genius he was to make the incomprehensible clear. Men of the highest distinction and world-wide fame have succeeded Hughlings-Jackson here, and any misgivings that I may feel as to the fate of the Society while for a year it is under my rule are put an end to by the knowledge that there are many left who have already done the best kind of work and who will in process of time adorn this chair. I thank you for the great honour you have done me in electing me President of the Neurological Society.

ANALYSIS OF 155 CASES OF TABES.

BY BYROM BRAMWELL, M.D., F.R.C.P.E., F.R.S.E.

Physician to the Edinburgh Royal Infirmary, &c , &c.

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Type of the disease: Sex: Age at onset· Married, widowed or single: Occupation.

Etiology: Syphilis; gonorrhœa; the length of time which elapsed between the occurrence of the venereal sore and the development of the tabes; sexual excess; marriage; alcoholic excess; injury; exposure to cold and wet; mental worry; excessive standing and bleeding piles; scarlet fever; diphtheria; constitution; neurotic inheritance.

The etiology of tabes; the relationship of syphilis and tabes.

Mode of onset; the length of time the disease had been in existence before the patients came under observation; the nature of the first symptoms.

Analysis of individual symptoms.

Lightning pains; pain in the back; girdle sensation; paræsthesiæ, nature of; anæsthesia in the legs, arms, trunk, face and head; analgesia in the legs, arms, trunk, face and head; thoracic and ulnar analgesia; Biernacki's sign; sensibility to heat and cold; the stereognostic sense.

Ataxic gait; Rombergism; incoordination in the legs; incoordination in the arms; the condition of the sense of movement (muscular sense) in the legs, in the arms; the muscular analgesia in the legs; hypotonia.

The condition of the knee-jerk; Achillis-jerk; the relationship between the Achillis-jerk and the knee-jerk; deep reflexes in the upper extremities; jaw-jerk; plantar reflex; the toe movement (Babinski's sign); cremasteric reflex; abdominal reflex; bladder reflex; peculiar sensations attending or following the act of micturition; rectal reflex; sexual reflex; the relative conditions of the cremasteric and sexual reflexes; paralysis.

The condition of the pupils; equality in size, size; shape and regularity of margins; contractility to light; contraction on accommodation; the Argyll-Robertson condition; optic atrophy; the influence of optic atrophy on the symptoms and course of the disease; diplopia; ocular paralyses; nystagmus; watering of the eyes.

Crises. Gastric; rectal; laryngeal; vesical; intestinal; sexual; nasal.

Trophic lesions in the bones and joints; vasomotor and trophic alterations in the skin and its appendages; herpetic eruptions; petechiæ and ecchymoses; dropping out of the teeth; perforating ulcer of the foot; ulceration of toes and corns; shedding of toe nails; thickening of toe nails; thickening of skin of soles.

Mental symptoms; hearing; taste; smell; headache; giddiness; sleep.

Considerable loss of weight; the condition of the heart; pulse frequency; temperature; the condition of the urine.

Complications. General paralysis of the insane; pulmonary; cardiac and arterial; digestive; urinary, &c.

Results, causes of death; total duration of the fatal cases.

Table showing the frequency and percentage of the different symptoms in the total 155 cases observed, and in those cases in which the condition of the special symptom under investigation is specifically stated in the notes.

ANALYSIS OF 155 CASES OF TABES DORSALIS.

In this communication I propose to analyse 155 cases of tabes dorsalis met with in private and hospital practice. The notes of the earlier cases are necessarily in some respects incomplete, but all the later cases have been very carefully, indeed exhaustively, studied. Further, I have endeavoured to follow out the cases and to bring them up to date. I am consequently able, in a considerable proportion of the 155 cases, to trace the course of the disease during a period of several years, and in most of the fatal cases to give the total duration and the immediate cause of death.

TYPE OF THE DISEASE.

One hundred and twenty, or 77·4 per cent., of the 155 cases were in the ataxic, and 35, or 22·5 per cent., cases were in the preataxic stage of the disease.

SEX.

One hundred and forty of the 155 cases, or 90·3 per cent., were males, and 15, or 9·6 per cent., were females.

The sex-frequency as given by different authorities varies:—

Gowers[1]:—"The proportion of males to females is 10 to 1." *Bonar*[2]:—In 286 cases of tabes, 242, or 84·6 per cent., were males, and 44, or 15·38 per cent., were females—a proportion of 6·5 males to 1 female. *Thomas*[3]:—In 111 cases of tabes from the Johns Hopkins Hospital, there were 97 males and 14 females, 12·6 per cent.—a proportion of 7 males to 1 female. *Riley*[4] observed 61 cases; they were all males. *Motschutkowski*[5] observed 1,662 cases; 1,538, or 92·5 per cent., were males, and 124, or 7·4 per cent., females.

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[1] "Diseases of the Nervous System," 3rd Edition, by Sir William Gowers, vol. i., p. 899.

[2] "A Study of the Cases of Tabes Dorsalis in Prof. M. Allen Starr's Clinic, Columbia University, from January, 1888, to January, 1901," by Dr. A. B. Bonar. *The Journal of Nervous and Mental Disease*, May, 1901, p. 259.

[3] "An Analysis of the Cases of Tabes in the Johns Hopkins Hospital and Dispensary from Its Opening in May, 1889, to December, 1898," by Dr. H. M. Thomas. *Bulletin of Johns Hopkins Hospital*, vol. x., 1899, p, 51.

[4] "A Summary of the Symptoms in 61 Cases of Locomotor Ataxia, with Additional Remarks," by Dr. W. H. Riley. *The Journal of Nervous and Mental Disease*, Sept., 1898, p. 679.

[5] "Klinisch-Statistische Untersuchung der Tabes dorsalis," von Professor Motschutkowski (1899, St. Petersburg). *Neurolog Centralblatt.*, 1900, p, 767.

Consequently, in 613 cases of tabes analysed by Bonar, Thomas, Riley, and myself, 540, or 88 per cent., were males, and 73, or 11·9 per cent., were females; and in the 2,275 cases analysed by Motschutkowski, Bonar, Thomas, Riley, and myself, 2,078, or 91·3 per cent., were males, and 197, or 8·6 per cent., were females.

AGE OF ONSET.

The age at which the first symptoms of tabes were said to have developed was noted in 151 of the 155 cases, and is shown in Table I.:—

Table I.—Age at Onset in 151 *Cases of Tabes.*

Between	20	and	30	years,	19	cases or	12 5	per cent.
,,	30	,,	40	,,	77	,,	50·9	,,
,,	40	,,	50	,,	35	,,	23·1	,,
,,	50	,,	60	,,	18	,,	11·9	,,
Above 60 years			..	..	2	,,	1·3	,,
					151	,,	99 7	,,

In the 151 cases in which the age at onset was ascertained, the disease commenced in 112 cases, or 74·1 per cent., between the ages of 30 and 50.

In one case (case 17), in which the patient not only denied syphilis and gonorrhœa, but stated that he had never been exposed to infection, in which there were no appearances indicative of syphilitic disease and in which there was no evidence of inherited syphilis, the disease commenced at the early age of 21. In one case (case 78), in which the symptoms were in every way typical, the disease commenced at the age of 66; and in another case (case 92), characterised by marked ataxia and Rombergism, no pains, loss of the knee-jerk and the Argyll-Robertson condition of the pupils, at the remarkably advanced age of 73.

With regard to the age of onset, Gowers states:—"The middle period of adult life is that in which locomotor ataxy usually commences. No less than half the cases begin between 30 and 40, one quarter between 40 and 50, and rather less than a quarter between 20 and 30. It rarely begins after 50, but I have

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once known it to develop at 66. Under 20 it is still more rare, but cases are met with as early as 10, and even in quite young children, the subjects of the cause next described."

The age at onset in 565 cases analysed by Bonar, Thomas, Riley and myself, is shown in Table II.

Table II.—Age at Onset in 565 Cases of Tabes.

	Bonar		Thomas.		Riley.		Bramwell.		Total Four Observers	
	No.	Per cent.	No.	Per cent	No.	Per cent	No.	Per cent.	No.	Per cent.
Between 10 and 20 years	1	·1	—	—	—	—	—	—	1	·1
,, 20 ,, 30 ,,	43	17·26	8	7	3	—	19	12 5	73	12·9
,, 30 ,, 40 ,,	100	40·16	41	38	29	—	77	50 9	247	43·9
,, 40 ,, 50 ,,	80	32	43	40	20	—	35	23·1	178	31·4
Above 50 years	25	10	15	14	6	—	20	13·2	66	11 6
	249	—	107	–	58	—	151	—	565	99·9

MARRIED, WIDOWED, OR SINGLE.

In 90 of the 155 cases the patients were married; in 12 cases widowers or widows; in 23 cases single; and in 30 cases the condition as regards marriage is not stated in the notes.

Consequently, in the 125 cases in which the condition as regards marriage is stated in the notes, 81·6 per cent. were either married or widowed at the time when the patients came under observation, and only 18·4 single.

These figures seem to suggest that married men are more liable to tabes than single men, and that married men who have had syphilis—for the majority of the patients had had syphilis—are more liable to tabes than single men who have had syphilis. (See also page 28.) The number of cases observed is, however, far too small to admit of definite conclusions.

OCCUPATION.

The occupations of the patients were very various and are shown in Table III.

Table III.—Showing the Occupation in 155 *Cases of Tabes.*

Accountant	1
Architect	1
Bank Agent	1
Blacksmith	2
Bookbinder	2
Brass-finisher	1
Bricklayer	1
Cabinet-maker	2
Cab Proprietor	1
Carter	1
Chemist	1
Clergyman	1
Clerk	5
Commercial Traveller	5
Confectioner	1
Cooper	1
Dairyman	1
Draper	1
Engineer	8
Flax-dresser	1
Fisherman	1
Fruiterer	1
Furnaceman	1
Furniture-packer	1
Gardener	1
Gentleman (private means)	6
Glass cutter	1
Grocer	3
Groom	2
Hairdresser	1
Hotel-keeper	2
Housewife, or living at home	14
Inland Revenue Officer	1
Insurance Agent	2
Ironmonger	1
Labourer	7
Land Agent	2
Lawyer	4
Lithographer	1
	90
Brought forward	90
Lorryman	1
Manufacturer	1
Manager Public Company	1
Mason	3
Medical Practitioner	3
Merchant	5
Merchant (Corn)	1
Merchant (Wine)	1
Miner	3
Organist	1
Painter (Coach)	2
Painter (House)	3
Painter-on-china	1
Plasterer	1
Police Officer	2
Porter	1
Press-reader	1
Railway Agent	1
Railwayman	1
Railway-foreman	1
Ranchman	1
Rivetter	1
Rubber-worker	1
Sadler	1
Sailor	3
Salesman	2
Saw Miller	1
Shoemaker	3
Soldier	3
Spinner	1
Stableman	1
Stationer	1
Stockbroker	2
Stoker	1
Street-singer	1
Tramwayman	1
Whisky Agent	1
Not stated	6
Total	155

It is a remarkable coincidence which shows, *firstly*, how cautious one should be in drawing conclusions from comparatively small figures, and, *secondly*, how special cases come in peculiar runs—that, in the first 140 cases of the series, there was no medical practitioner and no chemist. This suggested (1) that medical men and chemists are less liable to tabes than persons of other occupations, and (2) that the apparent diminished liability of doctors and chemists to tabes is perhaps due to the fact that medical students, doctors and chemists, when they acquire syphilis, knowing the subsequent risks and dangers which the disease entails, take care to go through a prolonged course of careful treatment. But these theoretical suppositions were entirely upset by the fact *that in the last 15 cases there were three medical practitioners and one chemist*, and, curiously enough, the three medical practitioners came under observation consecutively (case 145 was a chemist and cases 148, 149, and 150 were medical practitioners). A similar coincidence is mentioned by Thomas.[1]

> "It is interesting to note," he says, "that in the first 50 cases treated in the Dispensary there was but one woman, and that she was the 50th case. On the other hand, in the Wards, three out of the first five cases were women. This shows how very unreliable such statistics are unless a very large number of cases is recorded."

ETIOLOGY.

SYPHILIS.—In 88, or 56·7 per cent. of the 155 cases, there was a definite history of a venereal sore, with or without secondary symptoms, or the presence of unmistakable signs of syphilis on the surface of the body; in 5 cases, or 3·1 per cent., it was practically certain, from the family history (repeated miscarriages or still-born children, husband syphilitic, &c.), that the patient had had syphilis; in 9 cases, or 5·7 per cent., the history as regards syphilis was doubtful; in 43 cases, or 27.7 per cent., the patients definitely denied syphilis; and in 10 cases, or 6·4 per cent., the presence or absence of syphilis was not specifically mentioned in the notes.

GONORRHŒA.—In 26 cases, or 16·7 per cent. in which the patients definitely denied syphilis, they admitted gonorrhœa.

Consequently, in 114 of the 155 cases, or 73·5 per cent., there was a definite history of some form of venereal disease (a chancre, definite secondary or tertiary symptoms, or gonorrhœa); and in 5 other cases it is practically certain that the patients had had syphilis. It is practically certain, therefore, that in 119 of the 155 cases, or 76·7 per cent., the patients had had some form or other of venereal disease.

In one case in which syphilis was denied, the condition of the teeth suggested congenital syphilis.

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[1] *Loc. cit.*, p. 52.

Further, it cannot be doubted that in some (perhaps a considerable proportion) of the 43 cases in which the patients definitely denied syphilis that they had actually suffered from that disease. In several of the cases in which syphilis was ultimately admitted, the patients had, at first, emphatically denied that they had suffered from the disease (in several instances they wrote to me correcting their denial).

Again, the percentage of cases in which a definite history of syphilis was obtained, was considerably higher in the last than in the first half of the series, probably, I think—though this may of course be merely a coincidence—because more stringent enquiries were made as regards syphilis in the later cases. In the first 77 cases (taken chronologically) syphilis was admitted in 37 cases, or 48·9 per cent.; while in the last 78 cases, syphilis was admitted in 46 cases, or 58·9 per cent.

But, allowing for these sources of fallacy, I am convinced (so far as one can be convinced of any medical fact which does not come under one's own observation) that in many of the 43 cases in which syphilis was denied, the patients had *not* suffered from the disease.

I see no reason why other toxins (than the toxin which results from syphilis) may not lead to the production, or predispose to the production, of tabes. In one case (case 77), the only apparent cause was scarlet fever (and endocarditis), and in another (case 80)—and this was a case of true tabes and not of diphtheritic ataxic neuritis or pseudo-tabes —the disease seemed to be due to diphtheria.

In three at least of the cases, the syphilis had been treated very thoroughly for long periods of time with mercury. These cases undoubtedly show—and this is an important practical point from an insurance point of view—that prolonged and thorough mercurial treatment does not, in all cases, at all events, prevent the subsequent development of tabes.

In these statistics I have not attempted to discriminate between a true syphilitic (hard) chancre and a soft sore; for in many cases I have found it very difficult, and in some cases impossible, to get reliable information regarding the nature of the primary sore (whether hard or soft) and as to the occurrence of slight secondary symptoms long years before. Further, it is admitted that the soft sore may "carry" the syphilitic poison and be followed by secondary and tertiary symptoms. Possibly, also, the poison of the "soft" sore and of gonorrhœa may, as some authorities (Hitzig, Buzzard, Motschutkowski, &c.) have suggested, lead to the production of tabes.

Authorities differ as to the frequency of a history of syphilis in cases of tabes. A few writers (Mobius and Drummond) think all cases are syphilitic; others place the frequency of previous syphilis as high as 90 per cent. or more (Erb 90·35 per cent.; Fournier 90 per cent. or more; Hirt 90 per cent.); others about 75 per cent. (Mendel 75 per cent., Gowers[1] 75 per cent., Senator 70 per cent.); others much lower (Dana 50 per cent., Mozel 46 per cent., Eulenberg 36 per cent., Motschutkowski 36 per cent.).

Referring to the presence of *urethritis* in his cases, Motschutkowski[2] says:—Of 1,538 men with tabes, 1,501, or 98 per cent., had at a previous date suffered from urethritis; many of these had had more than one attack, so that these 1,501 had had 2,127 gonorrhœal infections.

THE LENGTH OF TIME WHICH ELAPSED BETWEEN THE OCCURRENCE OF THE VENEREAL SORE AND THE DEVELOPMENT OF THE TABES.

This point, which is of great importance from an Insurance point of view, was definitely determined in 79 of the total 155 cases; the results are shown in Table IV.

Table IV.—Time between Chancre and First Symptoms.

1 to 5 years	(inclusive)	in 11	cases, or	13·9	per cent.
5 ,, 10 ,,	,,	21	,,	26·5	,,
10 ,, 15 ,,	,,	21	,,	26·5	,,
15 ,, 20 ,,	,,	16	,,	20·2	,,
20 ,, 25 ,,	,,	7	,,	8·8	,,
25 ,, 30 ,,	,,	3	,,	3·7	,,
	Total ..	79	,,	99·6	,,

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[1] Gowers says:—"It is probable, indeed, that taking all cases, a causal proportion of three-quarters would be nearer the truth" than the 69 per cent. which his statistics from private practice (114 cases in 175 cases) show. ("Diseases of the Nervous System," 3rd Edition, vol. i., p. 446)

[2] "Klinisch-statistische Untersuchung der Tabes dorsalis," von Professor Motschutkowski (1899, St. Petersburg). *Neurolog. Centralblatt.*, 1900, p. 767.

In other words, the tabes developed in 32 of the 79 cases, or 40·5 per cent., within the first ten years after the syphilis; and in 47 cases, or 59·3 per cent., more than ten years after infection (in 37 cases, or 46·8 per·cent., between 10 and 20 years after infection; and in 10 cases, or 12·6 per cent., more than 20 years after infection).

The length of time which elapsed between the occurrence of the venereal sore and the first symptoms of tabes in 235 cases analysed by Bonar, Thomas and myself, in which this point is definitely stated, is shown in table V.

Table V.—Time between Chancre and First Symptoms in 235 Cases of Tabes.

	Bonar	Thomas.	Bramwell	Total Cases.	Percentage.
1 to 5 years	26	6	11	43	18·2
5 „ 10 „	28	10	21	59	25·1
10 „ 15 „	18	13	21	52	22·1
15 „ 20 „	22	10	16	48	20·4
20 „ 25 „	8	4	7	19	8·0
25 „ 30 „	6	4	3	13	5·5
More than 30 years	1	0	0	1	·4
Total ..	109	47	79	235	—

SEXUAL EXCESS.—In 10 of the 155 cases, marked sexual excess was admitted; but since the presence or absence of this form of excess was not particularly enquired for in all cases, it may have been present in a considerably larger proportion of cases.

In nine of the 10 patients who admitted marked sexual excess, there was a definite history of syphilis; and in one case syphilis was denied.

Motschutkowski considers sexual excess a most important factor in the production of tabes; he noted this cause in 1,220 cases (74·6 per cent.).

He also thinks trauma, infectious diseases, bodily exertion, chills, hereditary predisposition, *and only in the last place syphilis*, must be taken into consideration.

He states that in favour of the importance of sexual excesses, besides the frequency of urethritis in the histories of tabetic patients, already referred to, is the circumstance that tabes always begins in the period of sexual potency, in women neither before nor after the conclusion of the menstrual periods.

Motschutkowski explains the great number of syphilitics in the statistics of Fournier, Erb, and other authors on the ground that doubtful cases are included; among his own cases, besides the 36 per cent. who had certainly suffered from syphilis, there were 35·2 per cent. of doubtful cases, so that he, "if biassed," could speak of 71·2 per cent. (*Loc. cit.*).

MARRIAGE.—In seven of the 155 cases (in addition to the 10 cases in which sexual excess was admitted), marriage seemed to have a decided influence either in producing or aggravating the disease. In four cases the symptoms developed soon or immediately after marriage; and in three cases the symptoms were markedly aggravated by marriage.

In five of the seven cases in which marriage seemed to produce or accelerate the development of the disease, there was a definite history of syphilis; in one case, syphilis was probable; and one case doubtful.

ALCOHOLIC EXCESS.—In 10 of the 155 cases, marked excess as regards alcohol was admitted; the actual number was probably larger.

In seven of the 10 cases in which marked alcoholic excess was present, there was a definite history of syphilis; in one case syphilis was probable; in one case doubtful; and in one case definitely denied. In all of these 10 cases, the disease was without doubt true tabes and not alcoholic neuritis or pseudo-tabes.

INJURY.—In six cases, an injury or operation was blamed by the patient as the cause of the disease; but it is very doubtful if in any of these cases the injury was the real cause.

In four cases, the injury consisted in a fall on the back.

In the *first* case (Case 2), the symptoms had been in existence a year before the receipt of the injury. In the *second* case (Case 40), the injury had occurred 20 years previously, the patient stated that she had never been well since the injury, but the symptoms of tabes had only existed for 14 years (*i.e.*, had not developed until six years after the injury). In the *third* case

(Case 54), the injury had occurred nine years before the development of the tabetic symptoms. In the *fourth* case (Case 109), the injury had occurred six years before the development of the tabetic symptoms; in this case the patient was, two years before the onset of the disease, bitten by a mad dog and treated by the Pasteur method of inoculation.

In one case, the disease developed eight months after an injury to the chest and arm—the injury to the arm necessitated amputation. In one case, the disease developed three months after an operation for varicocele.

In five of the six cases in which an injury or operation was blamed by the patient as the cause of the disease, there was a definite history of syphilis; in the remaining case, the patient was a female and no definite history as regards syphilis was elicited.

EXPOSURE TO COLD AND WET; LYING OUT AT NIGHT.—This was blamed by the patient in six cases.

In four of these six cases, there was a definite history of syphilis; in one case syphilis was doubtful; and in one case definitely denied.

MENTAL WORRY.—This was said to be the cause in two cases.

In one of these cases, there was a definite history of syphilis; and in one case syphilis was doubtful.

EXCESSIVE STANDING AND BLEEDING PILES.—This was said to be the cause in one case.

SCARLET FEVER AND ENDOCARDITIS.—This was the only apparent cause in one case. In that case syphilis was definitely denied.

DIPHTHERIA.—This appeared to be the cause in one case. In that case syphilis was definitely denied.

CONSTITUTION: NEUROTIC INHERITANCE.—In many of the cases the patients were naturally very robust and strong and of fine muscular development. One patient, aged 50, looked much younger than his age. In two cases the patients had always been delicate and of poor physique; one of these had spinal curvature, the result of former caries. Three of the patients were of a highly neurotic and emotional nervous temperament. One patient was congenitally colour blind. One patient suffered, both before and after the onset of the tabes, from recurring attacks of insanity, necessitating confinement in an asylum. In one case the left leg was markedly shorter and smaller than the right, the result of an attack of poliomyelitis anterior acuta in childhood. One of the patients was the subject of hypospadias. In another case the testicles were completely undeveloped (infantile); this patient was married, was said to have erections, but had had no children. The mothers of three of the patients were highly neurotic; in one of these cases the patient's mother died in an asylum. One of the patients had an epileptic daughter.

The etiological factors detailed above are summarised in Table VI.:—

Table VI.—Showing the Chief Etiological Factors in 155 *Cases of Tabes.*

Chancre, with or without 2nd or 3rd symptoms, admitted	the only apparent cause	57	
	+ sexual excess	9	
	+ marriage*	5	
	+ alcoholic excess	7	
	+ injury	5	
	+ exposure to cold and wet	4	
	+ mental worry	1	
			88
Chancre, with or without 2nd or 3rd symptoms, probable	the only apparent cause	3	
	+ marriage*	1	
	+ alcoholic excess	1	
			5
Chancre, with or without 2nd or 3rd symptoms, doubtful	the only apparent cause	5	
	+ marriage*	1	
	+ alcoholic excess	1	
	+ exposure to cold and wet	1	
	+ mental worry	1	
			9
Syphilis denied	and no other apparent cause	38	
	but sexual excess	1	
	but alcoholic excess	1	
	but exposure to cold and wet	1	
	but scarlet fever	1	
	but diphtheria	1	
			43
Not noted or elicited			10
			155

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* In the cases in which marriage is suggested as a cause of the disease, the symptoms either developed soon after marriage or became greatly aggravated soon after marriage.

NOTE ON THE ETIOLOGY OF TABES: THE RELATIONSHIP OF SYPHILIS AND TABES.

Most authorities now admit that syphilis is the most important cause of tabes. I agree with this opinion, which is very strongly corroborated by statistics, and especially by Erb's statistics. Erb found that in 1,000 cases of tabes 90 per cent. had had syphilis, while only 20 per cent. of 6,000 cases of other forms of nervous disease had had syphilis. But while I believe that syphilis (or, perhaps, to speak cautiously, some form or other of venereal disease) is the most important cause of tabes, I am at the same time of opinion that it is not the only cause. On this point, and on the whole question of the etiology of tabes, I have little to add to the opinions which I expressed in the third edition of my book on the "Spinal Cord,"[1] published in 1895. I would now say:—

(1) That syphilis (and also perhaps the soft sore and gonorrhœa) *per se* cannot be regarded as the sole cause of tabes. Syphilis does not appear to be the immediate or exciting cause of the disease, in most cases at least. But, nevertheless, it must, in my opinion, be regarded as the most important cause of tabes.

(2) That the toxin or toxins produced by the syphilitic virus seem to have a widespread effect upon the nervous system, which predisposes it, or renders it liable, to be injuriously affected by other conditions (such as various forms of strain and irritation), which may, perhaps, be regarded as the immediate or exciting cause or causes of tabes. In other words, the syphilitic virus seems to make the nervous system more vulnerable to the conditions (irritations—due to intoxications of different forms; strains; exhaustions, &c.) which are, perhaps, the immediate or exciting cause of tabes.[1]

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[1] That general paralysis of the insane and, probably also, tabes, or perhaps it would be more correct to say some of the symptoms of these diseases, are due, or are in some cases due, to some form of intoxication, is suggested by the remarkable remissions and periods of apparent cure which are not uncommon in G.P.I., and to the ups and downs in the severity of the symptoms which are occasionally, though much less frequently, observed in cases of tabes.

(3) That this effect, so far as our present knowledge enables us to judge, seems to be more marked on the ingoing or afferent than upon the outgoing or efferent side of the nervous apparatus, and to be especially marked upon the posterior root-ganglia and their central and peripheral projections, including the sensory nerve-terminations in the muscles.

(4) That the effect which syphilis produces on the nervous system is no doubt greater in some persons than in others, and in some races than in other races.

(5) That it is possible that some other forms of toxin (than the toxin or toxins of syphilis), perhaps the toxins of soft sores and of gonorrhœa, may produce the same effect or a very similar effect on the nervous system as the toxin of syphilis, and so may probably, in some cases at least, be the primary (or predisposing) cause of the disease; in other words, may play the same *rôle* in the production of tabes that syphilis does.

(6) I see no reason to doubt that in some persons the nervous tissues are so constituted, either as the result of an inherited or original, or of an acquired peculiarity of constitution, that the direct or exciting causes of tabes (such as cord strain or irritation) may *in them* produce tabes in the absence of syphilis. Further, it is probable, I think, that even in persons whose nervous tissues are originally sound and normal, the direct or exciting causes of tabes (such as cord strain or irritation) may, if those causes are unusually severe or unduly prolonged, lead to the production of tabes in the absence of syphilis.

In short, in the etiology of tabes three great factors have, I think, to be chiefly taken into account, viz. :—

(1) The organic constitution, so to speak, of the nervous tissues of the individual—the vulnerability of the nervous tissues in each special case.

(2) Syphilis, the action of which should perhaps in most instances at least, be regarded more as a predisposing than as the direct or exciting cause of tabes.

(3) Nervous and cord strain or irritation (sexual excess, excessive standing, the irritation of toxins introduced *ab*

extra, auto-intoxication, alcoholic excess, exposure to cold and wet, traumatic injury, &c.), the action of which should perhaps be regarded, in most cases at least, as the exciting or immediate cause of the disease.

And I would consequently say :—

(*A*) Given an individual with a normal and non-vulnerable nervous system, for the production of tabes, syphilis and cord strain or irritation of some form or another, are usually necessary; but,

(*B*) If the cord strain or irritation is excessive and prolonged, it is probable, I think, that such an individual may, in the absence of syphilis, become tabetic.

(*C*) Given an individual with an abnormal and particularly vulnerable nervous system, cord irritation or strain, even if it is not especially severe and unduly prolonged, may probably, in some cases, lead to the production of tabes, even if there is no syphilis; and will, of course, be much more likely to do so if the individual is syphilitic.

(*D*) That tabes will be most easily and readily produced (*a*) when the nervous system is originally vulnerable; (*b*) when there is syphilis; and (*c*) when there is excessive and prolonged cord strain or irritation—*i.e.*, when all three causes are present in the same case.

If these views are correct it is obvious that the etiology of tabes is a much more complicated question than some writers have supposed, and that, in different cases, the *rôle* which the three great factors—(*a*) original constitution or vulnerability of the nervous system; (*b*) syphilis; (*c*) cord strain or irritation—play in the production of tabes, will vary considerably, and that these three great factors will be met with in different combinations in different cases.

MODE OF ONSET.

In 152 of the 155 cases the onset appeared to be more or less gradual; in three cases (36, 38, and 124) the symptoms developed very rapidly, *i.e.*, the onset was acute.

The following are brief notes of these cases :—

No. 1 (*Case* 36).—Male, aged 35, married, seen at E. R. I., March 13, 1901. Denies syphilis, but admits gonorrhœa, followed by falling out of hair, twelve years ago.

Eleven weeks ago, began to have occasional shooting pains in the legs; seven weeks ago felt a moist feeling in the feet and perineum, and rapidly lost control of the bowels; then, in the course of four days, rapidly lost power of controlling the movements of his legs.

When seen, gait markedly ataxic, could only walk with support; Rombergism marked: knee-jerks and Achillis-jerks lost; Argyll-Robertson pupil present; a well-marked band of thoracic analgesia; no ulnar analgesia; no analgesia, rather hyperalgesia, of the calf muscles; distinct hypotonia; marked shooting pains; sphincter trouble (bladder and rectum) marked; no diminution of sexual desire and power; no ataxia in arms; muscular sense very defective in legs; pinching ulnar nerve does not cause local pain, but produces tingling and twitching in the fingers.

No. 2 (*Case* 38).—Married woman, aged 39, admitted to E. R. I., January 4, 1893, suffering from typical tabes. No direct history of syphilis, but her husband subsequently came under my treatment for extensive gummatous ulceration of the palate. Her mother died in an asylum. Patient has been subject to megrim.

Three months ago began to have occasional incontinence of urine; ten weeks ago, shooting pains in the left buttock and thigh; one day, nine weeks ago, when out walking, began to stagger—the left leg, she says, suddenly failed her—the difficulty in walking rapidly became worse.

On admission, there was no loss of motor power and no muscular wasting. The gait was extremely ataxic, Rombergism was marked—had difficulty in standing even with the eyes open; the knee-jerks were absent; numbness in the feet, legs, thighs, and buttocks; some analgesia in the same parts; the right pupil did not react to light, but contracted actively to accommodation; the left pupil acted briskly both to light and accommodation (unilateral Argyll-Robertson pupil); considerable difficulty in micturition (forcing and occasional incontinence); marked constipation; marked lightning pains. Patient died eight years after the onset.

No. 3 (*Case* 124).—Man, aged 33, clerk, seen October 20, 1897, complaining of dimness of vision. Denies syphilis; teeth suggestive of congenital syphilis.

Three years ago had temporary ptosis of right eyelid. Quite well otherwise till three weeks ago, when his sight began to fail rapidly. No pains. Slight headache a week ago. Loss of sexual desire and power for six weeks.

On examination:—discs pale from commencing optic atrophy; pupils myotic, and presenting the Argyll-Robertson condition; paralysis of both external recti muscles; right knee-jerk absent, left normal; urination difficult and occasional incontinence; no constipation. Is duller mentally than he was before his illness commenced. No ataxia, no Rombergism.

Two months later (December 15, 1897), both knee-jerks were absent, and the optic atrophy was much more advanced.

THE LENGTH OF TIME THAT THE DISEASE (TABES) HAD BEEN IN EXISTENCE BEFORE THE PATIENTS CAME UNDER OBSERVATION.

This was definitely ascertained in 151 of the 155 cases, and varied from a few months in nine cases, to 25 years in two cases In the remaining four cases in which the exact duration of the disease when the patient first came under observation is not definitely stated, the period is stated in the notes to have been many years in two cases, and some years in two cases. The exact details are given in Table VII.

Table VII.—Duration of the Disease when the Patients were first seen.

Less than a year	9 cases	Brought forward	137
1 year	17 ,,	11 years	1 case
2 years	23 ,,	12 ,,	4 cases
3 ,,	18 ,,	14 ,,	1 case
4 ,,	24 ,,	15 ,,	1 ,,
5 ,,	13 ,,	16 ,,	2 cases
6 ,,	14 ,,	17 ,,	1 case
7 ,,	5 ,,	20 ,,	2 cases
8 ,,	8 ,,	25 ,,	2 ,,
9 ,,	3 ,,	Many years	2 ,,
10 ,,	3 ,,	Some ,,	2 ,,
	137		155

THE NATURE OF THE FIRST SYMPTOMS.

This is a point of considerable practical importance, *i.e.*, for the purposes of diagnosis in the early stages of the disease.

In 151 of the 155 cases, the nature of the first symptom was stated by the patient to be as follows:—

Table VIII.—Nature of the First Symptoms, as stated by the Patient, in 151 *Cases of Tabes.*

Lightning pains (alone)	82	cases, or	52·9	per cent.	of 151 cases.
Diplopia	13	,,	8·6	,,	,,
Ataxia	13	,,	8·6	,,	,,
Loss of vision	9	,,	5·9	,,	,,
Lightning pains and ataxia	6	,,	3·9	,,	,,
Derangements of urination	6	,,	3·9	,,	,,
Gastric crises	5	,,	3·3	,,	,,
Numbness in the feet	3	,,	1·9	,,	,,
Ataxia, pain in the back, and numbness of the feet	2	,,	1·3	,,	,,
Pain in the back and ataxia	1	case, or	·6	,,	,,
Coldness of feet	1	,,	·6	,,	,,
Weakness	1	,,	·6	,,	,,
Ataxia and loss of sexual desire and power	1	,,	·6	,,	,,
Ataxia and bladder trouble	1	,,	·6	,,	,,
Lightning pains and bladder trouble	1	,,	·6	,,	,,
Joint affection	1	,,	·6	,,	,,
Numbness in the feet and catching of the toes	1	,,	·6	,,	,,
Pain in the back and bladder trouble	1	,,	·6	,,	,,
Ataxia and cramps in the hands	1	,,	·6	,,	,,
Noise in the ear (like a singing bird)	1	,,	·6	,,	,,
Loss of sexual power and desire	1	,,	·6	,,	,,
Total cases	151				

It will be noted that lightning pains, either alone or in combination with some other symptoms, were the first symptoms in 89 cases, or 57·4 per cent., of the whole 151 cases. In four of the 155 cases, the nature of the initial symptoms is not stated in the notes.

ANALYSIS OF INDIVIDUAL SYMPTOMS.

I will now consider *seriatim* the different symptoms and signs of the disease, as manifested in the 155 cases under analysis.

LIGHTNING PAINS.

Lightning pains were present in some part or other of the body in 148 of the 155 cases, or 95·4 per cent., and were absent in seven cases only (Cases 7, 33, 72, 92, 110, 124, and 137), or 4·5 per cent.

In my experience, lightning pains are by far the most frequent of all the symptoms and signs of tabes, and are by far the most common initial symptom.

The distribution of the lightning pains is shown in Table IX.:—

Table IX.—Parts affected by the Lightning Pains.

Legs alone	63	cases, or	40·6	per cent.	of the 155 cases.
Legs and trunk	30	„	19·3	„	„
Legs, arms and trunk	29	„	18·7	„	„
Legs and arms	16	„	10·3	„	„
Legs, trunk, arms and head ..	7	„	4 5	„	„
Legs, trunk and head	3	„	1·9	„	„
Absent	7	„	4·5	„	„
	155		99·8		

It will thus be seen that in the 148 cases in which lightning pains were present, they were, in every case, felt in the legs, whether they occurred in other parts of the body or not.

In a very large proportion of the cases, the lightning pains were said to be worse during wet, damp, windy, changeable weather, or before a storm. In many cases they were said to be worse after the patient got warm in bed. In one case the pains were said to be worse in winter and spring. In one case the pains were worse if the patient was constipated. In one case riding and hunting were repeatedly observed to be the exciting cause of very severe lightning pains, requiring morphia for their relief. In one case the occurrence of the gastric crises was always followed by very severe pains in the legs. In one case sexual excitement "had a bad effect on the pains." In several cases marked hyperæsthesia was observed after the lightning pains at the seat of the pains. In four cases a herpetic eruption, and in two cases petechiæ, developed at the seat of the pains. In one case very severe shooting pains were referred to the left forearm and hand, which had been amputated eight years previously. In several cases the severity of the pains lessened as the disease progressed. In several cases in which optic atrophy developed, the severity of the pains lessened with the loss of sight; but this was by no means invariably the case. This point will be considered in more detail under the head of optic atrophy. In one case the pains were much worse in the arms and thorax than in the legs. In one case the patient complained of a throbbing, bursting feeling in the legs (rather than of shooting pains) when he got warm before a fire. In one case of "bruised" pains in the legs and elbows. In one case of a fixed pain in the right arm. In one case the pains were apparently rheumatic rather than true shooting (lightning) pains. In many of the cases the pains were very severe, "terrifically severe," and required large doses of morphia hypodermically for their relief. In most cases phenacetin in large doses, 20 grains repeated every hour, until 60 grains had been taken, relieved the pains.

In my cases, lightning pains appear to have been more frequent than in other series of cases which have been published. Thus Leimbach[1] found in 400 cases the frequency of lightning pains was 88·25 per cent.; Bonar[2] in 286 cases, 78·67 per cent.; Thomas[3] in 111 cases, 54 per cent.; Riley[4] in 61 cases, 88·6 per cent.; and Bramwell in 155 cases 95·4 per cent.

Gowers gives the frequency as 90 per cent: "Spontaneous pains are present in some degree in nine-tenths of the cases of tabes." ("Diseases of the Nervous System," 3rd edition, vol. 1, p. 450.)

PAIN IN THE BACK.

This was present in 45 of the 155 cases, or 29 per cent.; absent in 45 cases, or 29 per cent.; and not specifically mentioned in the notes in 65 cases, or 41·9 per cent.

Consequently, in the 90 cases in which pain in the back is specifically mentioned in the notes, it was present in 45, or 50 per cent., and absent in 45, or 50 per cent.

In one case in which there was a very severe and persistent pain under the left scapula, an aneurism of the descending thoracic aorta was found *post mortem*.

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[1] "Statistisches zur Symptomatologie der Tabes Dorsalis," by Dr. Rud. Leimbach. *Deutsche Zeitschrift für Nervenheilkunde*, Bd. vii., Abth. 5 u. 6, 1895, p. 493.

[2] "A Study of the Cases of Tabes Dorsalis in Prof. M. Allen Starr's Clinic, Columbia University, from January, 1888, to January, 1901," by Dr. A. B. Bonar. *The Journal of Nervous and Mental Disease*, May, 1901, p 267.

[3] "An Analysis of the Cases of Tabes in the Johns Hopkins Hospital and Dispensary from its Opening in May, 1889, to December, 1898," by Dr. H. M. Thomas. *Bulletin of Johns Hopkins Hospital*, vol 10, 1899, p. 51.

[4] "A Summary of the Symptoms in Sixty-One Cases of Locomotor Ataxia, with Additional Remarks," by Dr. W. H. Riley. *The Journal of Nervous and Mental Disease*, Sept., 1898, p. 679.

GIRDLE SENSATION.

This was present in 67 of the 155 cases, or 43·2 per cent.; absent in 31 cases, or 20 per cent.; and not specifically mentioned in the notes in 57 cases, or 36·7 per cent.

Consequently, in the 98 cases in which the presence or absence of the girdle sensation is mentioned in the notes, it was present in 67 cases, or 68·2 per cent., and absent in 31 cases, or 31·63 per cent.

Leimbach found the girdle sensation present in 31 per cent. of his cases; Bonar in 48·6 per cent.; Thomas in 24 per cent.; Riley in 63·9 per cent.; and Bramwell in 43·2 per cent.

PARÆSTHESIÆ.

Some form of paræsthesiæ was present in 103 of the 155 cases, or 66·4 per cent.; absent in 15 cases, or 9·7 per cent.; and the presence or absence of paræsthesiæ was not specifically mentioned in the notes in 37 cases, or 22·8 per cent.

Consequently, in the 118 cases in which the presence or absence of paræsthesiæ is specifically stated in the notes, paræsthesiæ of some form or another were present in 103 cases, or 87·2 per cent., and absent in 15 cases, or 12·7 per cent.

Leimbach found paræsthesia and numbness present in the legs in 64·5 per cent. of his cases; Bonar in 54·54 per cent.; Thomas in 40 per cent.; Riley in 86·8 per cent.; and Bramwell in 66·4 per cent.

The nature of the paræsthesiæ in the 103 cases in which they were present was as follows:—

Table X.—Nature of the Paræsthesiæ.

Numbness	40
Numbness, and pins and needles	3
Numbness, and coldness of the feet	13
Numbness, and ground felt soft	12
Numbness, pins and needles, cold feet, and ground felt soft	1
Numbness, pins and needles, and cold feet	6
Numbness, cold feet, and ground felt soft	6
Numbness, pins and needles, cold feet, and ground felt soft	7
Pins and needles, and cold feet	2
Pins and needles, cold feet, and ground felt soft	1
Cold feet	9
Cold feet, and ground felt soft	1
Ground felt soft	2
No paræsthesiæ	15
Presence or absence of paræsthesiæ not noted	37
	155

Consequently, in the 103 cases in which paræsthesiæ were present, numbness (in feet, legs, hands, &c.) was noted, either alone or in conjunction with other forms of paræsthesia, in 88 cases, or 85·4 per cent.; coldness of the feet (a feeling as if standing on snow, &c.) was noted, either alone or in combination with other forms of paræsthesia, in 45 cases, or 43·6 per cent.; "the ground felt soft" was noted (but probably present in a much larger proportion of cases), either alone or in combination with other forms of paræsthesia, in 30 cases, or 29·1 per cent.; and pins and needles was noted, either alone or in combination with other forms of paræsthesia, in 20 cases, or 19·4 per cent.

In the 103 cases in which the above forms of paræsthesia (numbness, pins and needles, cold feet, the ground felt soft) were present, the following forms of paræsthesiæ were also noted:—

Case 2.—"Feels as cold as lead in the small of the back."

Case 30.—"A damp, cold feeling about the testicles."

Case 33.—"Feels as if standing on the point of a stick."

Case 68.—"Feels as if standing on hard balls."

Case 83.—Great hyperæsthesia of the skin.

Case 86.—Very marked hyperæsthesia.

Case 88.—"Feels as if the intestines were enormously swollen up and as if there was a pillow between the legs."

Case 120.—"Pain in the groin and a feeling of dampness as of a discharge from the penis; this caused great mental distress."

Case 122.—Great hyperæsthesia of the abdomen, extreme sensitiveness to heat and cold.

Case 129.—Extreme hyperæsthesia of hands and arms; "if grasps anything, such as a window cord, feels as if the flesh were being stripped off."

Case 150.—Extreme hyperæsthesia of the skin of thorax.

ANÆSTHESIA IN THE LEGS.

In 68, or 43·8 per cent., of the 155 cases, there was more or less anæsthesia in the legs; in 46 cases, or 29 6 per cent., there was no anæsthesia in the legs; and in 41 cases, or 26·4 per cent., the presence or absence of anæthesia in the legs is not specifically mentioned in the notes.

Consequently, in the 114 cases in which the presence or absence of anæsthesia in the legs was specifically mentioned in the notes, it was present in 68 cases, or 59·6 per cent., and absent in 46 cases, or 40·3 per cent.

In many of the 68 cases in which anæsthesia was present in the legs, it was only slight and limited in its distribution.

ANÆSTHESIA IN THE ARMS.

In 20 of the 155 cases, or 12·9 per cent, there was more or less anæsthesia in the arms; in 54 cases, or 34·8 per cent., there was no anæsthesia in the arms; and in 81 cases, or 52·2 per cent, the presence or absence of anæsthesia in the arms is not specifically mentioned in the notes.

Consequently, in the 74 cases in which the presence or absence of anæsthesia in the arms was specifically mentioned in the notes, it was present in 20 cases, or 27 per cent., and absent in 54 cases, or 72·9 per cent.

ANÆSTHESIA IN THE TRUNK.

In 40 of the 155 cases, or 25·8 per cent., there was more or less anæsthesia in the trunk; in 35 cases, or 22·5 per cent., there was no anæsthesia in the trunk; and in 80 cases, or 51·6 per cent., the presence or absence of anæsthesia in the trunk is not specifically mentioned in the notes.

Consequently, in the 75 cases in which the presence or absence of anæsthesia in the trunk was specifically mentioned in the notes, it was present in 40 cases, or 53·3 per cent., and absent in 35 cases, or 46.6 per cent.

ANÆSTHESIA IN THE FACE.

In two of the 155 cases, or 1·2 per cent,, there was more or less anæsthesia in the face; in 56 cases, or 36·1 per cent., there was no anæsthesia in the face; and in 97 cases, or 62·5 per cent., the presence or absence of anæsthesia in the face is not specifically mentioned in the notes.

Consequently, in the 58 cases in which the presence or absence of anæsthesia in the face was specifically mentioned in the notes, it was present in two cases, or 3·4 per cent., and absent in 56 cases, or 96·5 per cent.

In one case (53) there was complete anæsthesia and analgesia of one—the left—side of the face and tongue, obviously due to a lesion of the fifth nerve or its central connections.

In one case (21) there was complete hemianæsthesia and hemianalgesia of the left side of the body (face, arm and leg).

In another case (90) the presence of temporary hemianæsthesia and hemianalgesia was noted. I have not included this case, since in it the hemianæsthesia was merely a temporary and functional condition.

ANALGESIA IN THE LEGS.

In 55, or 35·4 per cent. of the 155 cases, there was more or less analgesia in the legs; in 36 cases, or 23·2 per cent., there was no analgesia in the legs; and in 64 cases, or 41·2 per cent., the presence or absence of analgesia in the legs is not specifically mentioned in the notes.

Consequently, in the 91 cases in which the presence or absence of analgesia in the legs was specifically mentioned in the notes, it was present in 55 cases, or 60·3 per cent., and absent in 36 cases, or 39·6 per cent.

ANALGESIA IN THE ARMS.

In 40, or 25·8 per cent. of the 155 cases, there was more or less analgesia in the arms; in 32 cases, or 20·6 per cent., there was no analgesia in the arms; and in 83 cases, or 53·5 per cent., the presence or absence of analgesia in the arms is not specifically mentioned in the notes.

Consequently, in the 72 cases in which the presence or absence of analgesia in the arms was specifically mentioned in the notes, it was present in 40 cases, or 55·5 per cent., and absent in 32 cases, or 44·4 per cent.

ULNAR ANALGESIA.

In the last 60 cases of the series, which were examined with special care and detail, ulnar analgesia was present in

29, or 48·3 per cent., absent in 23, or 38·3 per cent., and not specifically mentioned in the notes in 8, or 13·3 per cent.

Leimbach found ulnar paræsthesia in 16·5 per cent. of his cases.

BIERNACKI SIGN.

In the last 60 cases of the series Biernacki's sign—absence of pain on irritation (pinching) of the ulnar nerve at the elbow—(and in some cases absence of tingling) was present in 14 cases, or 23·3 per cent.; absent in 9 cases, or 15 per cent., and not specifically mentioned in the notes in 37 cases, or 61·6 per cent.

ANALGESIA IN THE TRUNK, THORAX AND ABDOMEN.

In 59 of the 155 cases, or 38 per cent., there was more or less analgesia in the trunk; in 19 cases, or 12·2 per cent., there was no analgesia in the trunk; and in 77 cases, or 49·6 per cent., the presence or absence of analgesia in the trunk is not specifically mentioned in the notes.

Consequently, in the 78 cases in which the presence or absence of analgesia in the trunk was specifically mentioned in the notes, it was present in 59 cases, or 75·6 per cent., and absent in 19 cases, or 24·3 per cent.

THORACIC ANALGESIA.

In he last 60 cases of the series, which were examined with special care and detail, thoracic analgesia was present in 45 cases, or 75 per cent., and absent in 15 cases, or 25 per cent.

ANALGESIA IN THE FACE AND HEAD.

In 2 of the 155 cases, or 1·2 per cent., there was more or less analgesia in the face and head; in 51 cases, or 32·9 per cent., there was no analgesia in the face and hoad; and in 102 cases, or 65·8 per cent., the presence or absence of analgesia in the face and head is not specifically mentioned in the notes.

Consequently, in the 53 cases in which the presence or absence of analgesia in the face and head was specifically mentioned in the notes, it was present in 2 cases, or 3·7 per cent., and absent in 51 cases, or 96·2 per cent.

SENSIBILITY TO HEAT AND COLD.

This was only carefully investigated in such a small number of the 155 cases, that I am not able to make any definite and reliable statement regarding its condition.

THE STEREOGNOSTIC SENSE.

This was examined in a few cases only; in one case (39) it was defective, in all the other cases in which it was examined it was unaffected.

ATAXIC GAIT.

In 120 of the 155 cases, or 77·4 per cent., an ataxic gait was present; and in 35 cases, or 22·5 per cent., absent.

In three cases the ataxia was very rapidly developed (36, 38, 71).

In one case—an undoubted case of true tabes, the patient stated that he was able to walk better in the dark than in the light; he was a very nervous man and felt his ataxic inability much worse in the streets, in crowded places, &c.

In several of the cases, the patients stated that they had special difficulty in going down stairs. In one case (87), the patient stated that he had much greater difficulty in going up than down stairs.

Several of the patients stated that they were able to walk much better on soft ground, on grass or turf. One patient had provided himself with india-rubber heels; and acting on the hint which he gave me, I have prescribed india-rubber soles or heels, with great benefit, for several of my patients. I have found that, in many cases in which the ataxia was very marked, the patients could walk much better in india-rubber soles than in ordinary boots. Sticks tipped with india-rubber are also much better than sticks with iron ferrules for those ataxics who require to use sticks.

One patient, a commercial traveller, who was markedly ataxic and who had suffered from the disease for 11 years, travelled 8,000 miles in the course of the year and did a very large business.

ROMBERGISM (INABILITY TO STAND STEADILY WITH THE EYES CLOSED).

In 120 of the 155 cases, or 77·4 per cent., Rombergism was present; in 34 cases, or 21·9 per cent., absent; and in 1 case, or ·6 per cent., the presence or absence of Rombergism was not specifically mentioned in the notes.

Leimbach observed Rombergism in 88·75 per cent. of his cases; Bonar in 79 per cent.; Thomas in 76·6 per cent.; Riley in 88·5 per cent.; Bramwell in 77·4 per cent.

INCOORDINATION IN THE LEGS.

In 117, or 75·4 per cent., of the 155 cases, incoordination was present in the legs; in 35, or 22 5 per cent., incoordination was absent in the legs; and in 3, or 1·9 per cent., the presence or absence of incoordination in the legs (other than the incoordination shown by the ataxic gait) is not specifically mentioned in the notes.

Consequently, in the 152 cases in which the presence or absence of incoordination in the legs is specifically mentioned in the notes, it was present in 117 cases, or 76·9 per cent., and absent in 35 cases, or 23 per cent.

In two cases the ataxia was much more marked in one leg than in the other.

Leimbach noted ataxia in the legs in 74·75 per cent. of his cases; Bonar in 70·62 per cent.; Thomas in 80·1 per cent.; Riley in 67·2 per cent.; Bramwell in 75·4 per cent.

INCOORDINATION IN THE ARMS

In 39, or 25·1 per cent., of the 155 cases, incoordination was present in the arms; in 69 cases, or 44·5 per cent., there was no incoordination present in the arms; and in 47 cases, or 30·3 per cent., the presence or absence of incoordination in the arms is not specifically mentioned in the notes.

Consequently, in the 108 cases in which the presence or absence of incoordination in the arms is definitely stated in the notes, it was present in 39 cases, or 36·1 per cent., and absent in 69 cases, or 63·9 per cent.

In 22 of the 39 cases in which there was incoordination in the arms, it was very slight; it was only in 17, or 10·9 per cent. that the ataxia in the arms was at all marked. In one case only (123) was the ataxia and loss of the muscular sense extremely marked in the arms.

The presence or absence of ataxia in the arms was judged of by the patient's ability to touch the tip of the nose with certainty with the forefinger, the eyes being closed. My observations seem to show that if this test is carefully employed; ataxia in the arms, in a slight form, will be found in a very much larger proportion of cases of tabes than most authorities allow.

Leimbach observed ataxia in the arms in 4·2 per cent only of his cases; Bonar in 7·69 per cent.; Thomas in 11·7 per cent.; Riley in 24·5 per cent.; Bramwell in 25·1 per cent.

THE CONDITION OF THE SENSE OF MOVEMENT (MUSCULAR SENSE) IN THE LEGS.

In 67 of the 155 cases, or 43·2 per cent., the sense of movement (as judged by the patient's ability to estimate the difference between weights, the direction of passive movements and the position of the limbs after passive movements) was affected; in 30 cases, or 19·3 per cent., unaffected; and in 58 cases, or 37·4 per cent., the condition of the sense of movement in the legs was not specifically mentioned in the notes.

Consequently, in 97 cases in which the sense of movement in the legs is specifically stated in the notes, it was impaired in 67, or 69 per cent., and not affected in 30, or 30·9 per cent.

In nine cases (Cases 16, 21, 32, 39, 45, 71, 96, 105, 106) the ataxia and loss of the muscular sense were extreme, the patients being totally unable to tell the position of the limbs when the eyes were closed. In two of these cases, there was practically little or no impairment of the tactile sensibility.

In one case in which there was marked ataxia and loss of the sense of movement in the legs, the patient was, once he got into the saddle, able to ride a bicycle

THE CONDITION OF THE SENSE OF MOVEMENT (MUSCULAR SENSE) IN THE ARMS.

The sense of movement in the arms was affected in 24 of the 155 cases, or 15·4 per cent.; unaffected in 52, or 33·5 per cent; and not specifically mentioned in the notes in 79 cases, or 50·9 per cent.

Consequently, in the 76 cases in which the condition of the sense of movement in the upper extremities is specifically stated in the notes, it was affected in 24, or 31·5 per cent., and unaffected in 52, or 68·4 per cent.

In the great majority of the 24 cases in which the sense of movement in the arms was affected, the impairment was only slight.

MUSCULAR ANALGESIA IN THE LEGS.

This was present in 38 of the 155 cases, or 24·5 per cent.; absent in 16 cases, or 10·3 per cent.; and not specifically mentioned in the notes in 101 cases, or 65·1 per cent.

Consequently, in the 54 cases in which the presence or absence of muscular analgesia in the legs was mentioned in the notes, it was present in 38 cases, or 70·3 per cent., and absent in 16 cases, or 29·6 per cent.

In 2 cases in which there was most marked muscular analgesia in the calves, there was no ataxia or incoordination and no loss of muscular sense (the sense of movement) in the legs. This is a point of considerable interest in connection with the pathological physiology of the ataxia.

MUSCULAR HYPOTONIA.

This was present in 38 of the 155 cases, or 24·5 per cent.; absent in 9 cases, or 5·8 per cent.; and not noted in 108 cases, or 69·6 per cent

Consequently, in the 47 cases in which the presence or absence of hypotonia was mentioned in the notes, it was present in 38 cases, or 80·8 per cent., and absent in 9 cases, or 19·1 per cent.

In many of the cases in which hypotonia was present it was only slight.

Note.—Hypotonia in the legs was regarded as present when the patient, lying flat on the back, the extended leg could be brought to a right angle, or less than a right angle, with the trunk.

THE CONDITION OF THE KNEE-JERKS.

In 127 of the 155 cases, or 81·9 per cent., the knee-jerks were lost; in 20 cases, or 12 9 per cent., the knee-jerks were present either on one or both sides. In 8 cases, or 5·1 per cent., the condition of the knee-jerks is not specifically mentioned in the notes.

Of the 20 cases in which the knee-jerk was present, it was present on one side only in six cases (56, 69, 75, 90, 124, 145), or 3·8 per cent., and on both sides in 14 cases, or 9 per cent. In five of these cases it was exaggerated.

In five of the 20 cases in which the knee-jerks were present on one or both sides when the patient first came under observation, they were subsequently lost as the disease progressed (cases 26, 56, 62, 116, 124).

In *Case* 26 the knee-jerks were obtained with reinforcement on October 20, 1893, but were completely absent on March 27, 1894, and on December 31, 1900.

In *Case* 56 the left knee-jerk was absent, the right very slight on April 13, 1899, and both completely lost on December 24, 1900.

In *Case* 62 the knee-jerks were present on January 30, 1900, and lost on July 9, 1900.

In *Case* 116 the knee-jerks were active on July 28, 1896, but completely absent on December 4, 1900.

In *Case* 124, on October 20, 1897, the right knee-jerk was absent, the left normal; on December 15, 1901, both knee-jerks were lost.

The knee-jerks were, therefore, ultimately lost in 132 cases, or 85·1 per cent. of the 155 cases.

In two cases in which the knee-jerks were absent when the patients were first seen, they returned as the case progressed (Cases 25, 108). In both cases they were subsequently again lost.

In seven of the cases in which the knee-jerks were present they were very active in two cases (Cases 37, 116) and exaggerated on one or both sides in five cases (Cases 15, 43, 63, 128, 140).

I need hardly add that the cases in which the knee-jerks were exaggerated were cases of true tabes—not cases of ataxic paraplegia.

Consequently, in the 147 cases in which the condition of the knee-jerks is specifically stated in the notes, they were absent when the patient first came under observation in 127 cases, or 86·3 per cent., and ultimately lost in 132 cases, or 89·7 per cent.

Leimbach found the knee-jerks lost in 92·2 per cent. of his cases; Bonar in 90·9 per cent; Thomas in 81 per cent.; and Riley in 90·1 per cent.; Bramwell in 85·1 per cent.

The exact frequency (percentage) with which the knee-jerk is absent in any series of cases of tabes will, of course, to some extent depend upon the relative proportion of the cases of preataxic and ataxic in that series.

A few years ago many observers would probably have excluded those cases or some of the cases of preataxic tabes in which the knee-jerks were present. Consequently, it is, I think, certain that in the future (since the diagnosis of preataxic tabes has become more exact, and since we now recognise many obscure cases as cases of preataxic tabes which were not recognised as tabes a few years ago) the percentage of cases of tabes in which the knee-jerks are lost will be found to be somewhat less than in the series of cases collected a few years ago. This is, probably, the explanation of the fact that in my series of cases the knee-jerks were lost in a somewhat smaller percentage of cases—85·1—than in the series of cases recorded by Leimbach, Bonar, and Riley.

ACHILLIS-JERK.

In 44 of the 155 cases, or 28·3 per cent., the Achillis-jerk was absent on one or both sides (in two of these cases, or 1·3 per cent., on one side only; and in 42, or 27 per cent., on both sides); in eight cases, or 5·1 per cent., the Achillis-jerk was present on both sides; in 103 cases, or 66·4 per cent., the Achillis-jerk was not examined.

Consequently, *in the* 52 *cases in which the Achillis-jerk was examined*, it was absent in 44 cases, or 86·4 per cent., on one or both sides (on both sides in 42 cases, or 80 7 per cent.; and in two cases, or 3·8 per cent., on one side); and in eight cases or 15·3 per cent., it was present on both sides.

Leimbach found the Achillis-jerk absent in 92 per cent. of his 400 cases of tabes (the same percentage as the absence of the knee-jerk).

A comparison of the frequency with which the knee-jerks and the Achillis-jerks were absent in the 147 and 52 cases respectively in which these jerks were noted, shows that the knee-jerks were absent in 89·7 per cent., and the Achillis-jerks in 86·4 per cent. The greater frequency with which the knee-jerks were absent was without doubt, I think, due to the fact that in the 52 cases in which the Achillis-jerks were examined, there was a larger number (proportion) of cases of preataxic tabes than in the 147 cases in which the knee-jerks were examined.

In the 52 cases of tabes in which *both* the knee-jerks and the Achillis-jerks were examined, the knee-jerks were absent in exactly the same percentage as the Achillis-jerks, viz., 86·4 per cent.

THE RELATIONSHIP BETWEEN THE ACHILLIS-JERKS AND THE KNEE-JERKS.

In the 41 cases in which the Achillis-jerks were absent on both sides, the knee-jerks were also absent on both sides.

In seven of the eight cases in which the Achillis-jerks were present on both sides, the knee-jerks were also present on both sides.

Consequently, in 48 of the 52 cases in which the Achillis-jerks were examined, the condition of the Achillis-jerks and knee-jerks was the same. In the remaining four cases, the Achillis-jerks and knee-jerks were not affected in the same way.

In Case 43, the Achillis-jerk was present on the right side, absent on the left side, while the knee-jerks were present on both sides.

In Case 60, the Achillis-jerk was present on the right side, absent on the left side, while the knee-jerk was absent on both sides.

In Case 69, the Achillis-jerk was present on both sides, while the knee-jerk was absent on the right side and exaggerated on the left.

In Case 145, the Achillis-jerks were absent on both sides, and the knee-jerk was absent on the right side, but obtained by reinforcement on the left side.

The condition in these exceptional cases is diagrammatically represented in the following table:—

Table XI.—The Condition of the Achillis-jerks and Knee-jerks in four cases of Tabes, in which the two jerks were not affected in the same way.

No. of Case.	Left Leg.		Right Leg.	
	Knee-jerk.	Achillis-jerk.	Knee-jerk.	Achillis-jerk.
Case 48	normal	absent	normal	normal
,, 60	absent	absent	absent	normal
,, 69	exaggerated	exaggerated	absent	exaggerated
,, 145	present on reinforcement	absent	absent	absent

DEEP REFLEXES—UPPER EXTREMITIES.

In 23 of the 155 cases, or 14·8 per cent., the deep reflexes in the upper extremities were absent, or not obtained,[1] on one or both sides (in one case on one side and in 22 cases on both sides); in 22 cases, or 14·1 per cent., present on both sides; and in 110 cases, or 70·9 per cent., the presence or absence of the deep reflexes is not recorded in the notes.

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[1] I say not obtained, for in some cases it is difficult to obtain these reflexes, especially the triceps jerk, in health.

Consequently, in 23, or 50·9 per cent., of the 45 cases in which the condition of the deep reflexes in the upper extremities was noted, they were absent or not obtained on one or both sides; and in 22 cases of the 45, or 48·9 per cent., they were present on both sides.

In four of the cases in which the deep reflexes were present in the upper extremities, they were exaggerated.

In the first case (63), the patient was affected with pre-ataxic tabes, and was examined after a severe and prolonged gastric crisis, the knee-jerks and Achillis-jerks were exaggerated; the Argyll-Robertson pupil was present.

In the second of these four cases (64), the patient was the subject of G. P. I.; in that case the Achillis-jerks and knee-jerks were absent.

In the third case (143), the patient was the subject of pre-ataxic tabes, the knee-jerks and Achillis-jerks were exaggerated, the pupils were unequal in size and myotic, but contracted to light. The patient had had syphilis. For eight years he had suffered from severe lightning pains, he had had diplopia, there was some (slight) ulnar analgesia.

In the fourth case (145), the disease was in the pre-ataxic stage, the Achillis-jerks were both absent, the knee-jerk was absent on the left side, but present, after reinforcement, on the right.

Bonar found the arm-jerks absent in 13, or 4·5 per cent. of his 286 cases, in all the other cases they were present or not recorded. Leimbach gives no exact figures.

JAW-JERK.

In seven, or 4 5 per cent., of the 155 cases, the jaw-jerk was absent; in 32, or 20·6 per cent., present; and in 116, or 74 8 per cent., not specifically mentioned in the notes.

Consequently, in the 39 cases in which the condition of the jaw-jerk is specifically mentioned in the notes, it was absent (or not obtained) in seven cases, or 17·9 per cent., and present in 32 cases, or 82 per cent.

In three of the 32 cases in which the jaw-jerk was present it was exaggerated (Cases 64, 65 and 145); one of the patients (Case 64) was the subject of G. P. I.; one of the patients (Case 65) had previously had two attacks of hemiplegia, one on the right, the other on the left, side—in this case the arm-jerks were not obtained on the left and were only slight on the right side; one of the patients (145) was in the pre-ataxic stage of the disease.

Plantar Reflex.

In 19 of the 155 cases, or 12·2 per cent., the plantar reflex was absent; in 97 of the 155 cases, or 62·5 per cent., the plantar reflex was present on one or both sides; in 95 cases on both sides, and in two cases on one side only; and in 39 cases, or 25·1 per cent., the condition of the plantar reflex is not specifically mentioned in the notes.

In 32 of the 97 cases in which the plantar reflex was present, it was exaggerated.

Consequently, in the 116 cases in which the condition of the plantar reflex was noted, it was present on one or both sides in 97 cases, or 83·6 per cent. (on one side only in 2 cases, or 1·7 per cent.; and on both sides in 95, or 81·9 per cent.). In 19, or 16 3 per cent., of the 116 cases in which the condition of the plantar reflex was noted, it was absent. In 32 of the 116 cases, or 27·5 per cent., in which the condition of the plantar reflex was specifically stated in the notes, it was exaggerated—often extremely so. This exaggeration of the superficial reflexes in tabes is, I think, of some diagnostic importance, more especially in the early stages of ill-developed cases.

In one case (21), there was a quite extraordinary exaggeration of the plantar reflex; in that case, too, the delay in the reflex—the period between the irritation of the sole and the muscular contraction which resulted therefrom—was very remarkable. The details are as follows:—

Case 21.—Male, aged 42, married, an old soldier, was seen in the Craiglockhart Poorhouse with Dr. Carmichael on November 15, 1900, and on several subsequent occasions.

The disease was of six years' duration. The patient denied syphilis. The leading features of the case were:—Severe and frequently recurring lightning pains, extreme ataxia in the legs, slight ataxia in the arms; loss of the knee-jerks; complete blindness and optic atrophy; double Argyll-Robertson pupil; difficulty in urination; no constipation; complete loss of sexual desire and power; girdle sensation; complete left-sided hemianæsthesia and analgesia (skin, mucous membranes, and special senses); slight anæsthesia and analgesia in the right arm, right side of the thorax and abdomen, and right thigh; marked anæsthesia and analgesia in the right leg (below the knee); complete loss of the muscular sense and the sense of position of the limbs during and after passive movements in both lower extremities; absence of the cremasteric and abdominal reflexes; muscles of the lower extremities firm and well developed; complete inability to move the left leg while lying in bed, and almost complete inability to move the right leg; ability to move the legs in a wildly incoordinate way when supported on each side in the erect position, but only knows that he is moving the legs by the noise which the feet make in coming in contact with the floor; absence of the plantar reflex in the left leg; remarkable reflex spasm in the head and upper part of the body produced, after a very long latent interval, on tickling the sole of the right foot.

The following are the notes which I made of the condition of the plantar reflex in this very remarkable case:—

The plantar reflex is absent on the left side. Scratching the right sole with the blunt end of a tuning-fork is attended with a very remarkable result. A very slight, slow scratch is followed after an interval of three or four seconds by a clonic movement of the right leg. A more powerful (sharp) scratch is followed after an interval of several seconds by a sudden and very violent spasmodic movement of the head and upper part of the body, which almost throws the patient out of bed; the legs are stiffly extended and the upper part of the body and head violently jerked, the head coming violently in contact with the top of the bed; the bed was much shaken, and the sudden movement, following the scratching of the sole after what appeared to be a very long interval, gave me and Dr Carmichael and the nurse who witnessed it a great start. The observation was repeated several times, both on the same day and at subsequent visits, and always with exactly the same result. The patient felt shaken and exhausted after the spasm, and finally begged us not to repeat it. I have never seen anything at all comparable to it.

The following are two additional illustrations of great exaggeration of the plantar reflex:—

Case 15.—Labourer, aged 59, seen at the Edinburgh Royal Infirmary on June 27, 1888. Duration of the disease five years Syphilis denied. First symptom lightning pains in the legs. *Present state* :—Severe and highly-typical lightning pains in the legs; marked ataxia and Rombergism; double Argyll-Robertson pupil; knee-jerks very active on both sides; typical and severe gastric crises, frequently recurring; great exaggeration of the superficial reflexes—a scratch on the sole was followed after a considerable interval (great delay in the reflex interval) by marked clonic tremors, continuing for some time, in the leg on the same side. There is no statement in the notes of the condition of the urinary, rectal, and sexual reflexes.

Case 16.—Spinner, aged 48, seen at the Edinburgh Royal Infirmary on June 1, 1889. Duration of the disease 2½ years. Syphilis denied. First symptom, difficulty in walking and pain in the back. Present state :—Severe and frequently recurring lightning pains in the legs and arms; coldness of the feet; pain at the bottom of the back; marked girdle-pain; great ataxia: marked Rombergism; great impairment of the muscular sense in the lower extremities, after passive movements with the eyes closed, the patient is completely ignorant of the position of the lower extremities: loss of the knee-jerks; pupils myotic, double Argyll-Robertson pupil present; analgesia of the soles and marked impairment of the tactile sensibility in the lower extremities; urination very markedly affected; obstinate constipation; complete loss of sexual desire and power; cremasteric reflex absent; great exaggeration of the plantar reflex on each side—a scratch on either sole with the blunt end of a tuning-fork was followed after a long interval (marked delay) by violent clonic movements, which continued for some time after the irritation, in both legs.

The patient died two years subsequently; total duration of the disease 4½ years; death certificate "Locomotor ataxia and asthma."

In one case, irritation of (tickling) the soles was always followed by a slow drawing up of the legs, flexion of the thigh on the abdomen. This patient was quite unable, from flaccid paralysis, to make any voluntary movement in the lower extremities.

THE TOE MOVEMENT: BABINSKI'S SIGN.

In 47 of the 155 cases, the condition of the toe movement was noted. In three cases, or 6·3 per cent. of these 47 cases, there was no movement of the toes; in 39 cases, or 82·9 per cent., the movement of the toes was flexion; and in five cases, or 10·6 per cent., extension on one or both sides.

In the first of the five cases in which Babinski's sign was present (Case 56), well-marked extention of the big toe was repeatedly noted on the left side and occasionally on the right. No cause was apparent for the Babinski sign.

In the second (Case 65), there was a marked double extensor response, which was satisfactorily accounted for by the fact that the patient had had two hemiplegic attacks, one (11 years previously) on the right, and the other (two years previously) on the left side.

In the third (Case 69), in which a double extensor response was present, the case was a difficult and complicated one, only to be explained by supposing that in addition to the tabes there were other cord lesions.

In the fourth (Case 73), the patient had, in addition to the tabes, symptoms and signs of cerebral syphilis. On admission, the toe movement was flexion, but on several subsequent occasions extension was noted.

In the fifth (Case 143), which was one of very early preataxic tabes, the toe movement in the left foot was slight extension; while in the right there was little or no toe movement, but what there was seemed to be extension rather than flexion.

In addition, in one well-marked case of tabes in which a slight and temporary hemiplegia developed during the patient's stay in hospital, the toe movement on the paralysed side, which had previously been flexion, became *for a time* extension.

The result of these observations is to show that the Babinski sign is only present in a small proportion of the cases of tabes, and that in those cases in which it is present, it is not due to the tabes, but is the result of some associated lesion or complication. I have only seen two cases of tabes in which the Babinski sign was present and in which its presence could not be satisfactorily accounted for by the presence of some associated lesion or complication.

CREMASTERIC REFLEX.

In 30 of the 155 cases, or 19·3 per cent., the cremasteric reflex was absent; in 55, or 35·4 per cent., present on one or both sides (in 50 on both and in five on one side only); and in 70, or 45·1 per cent., the condition of the cremasteric reflex is not specifically mentioned in the notes.

Consequently, in the 85 cases in which the condition of the cremasteric reflex is specifically noted, it was present on one or both sides in 55, or 64·7 per cent. (on both sides in 50 cases, or 58·8 per cent., and on one side only in five cases, or 5·8 per cent.) ; and was absent in 30 cases, or 35·2 per cent.

ABDOMINAL REFLEX.

In 55 cases, or 35·4 per cent., the abdominal reflex was present (in 53 cases on both sides, and in two cases on one side only); in 13 of the 155 cases, or 8·3 per cent., the abdominal reflex was absent; and in 87, or 56·1 per cent., the condition of the abdominal reflex is not specifically mentioned in the notes.

Consequently, in the 68 cases in which the condition of the abdominal reflex is specifically mentioned in the notes, it was present in 55 cases, or 80·8 per cent. (in 53 cases, or 77·9 per cent., on both sides, and in two cases, or 2·9 per cent., on one side only) ; and in 13 cases, or 19·1 per cent., it was absent.

In nine of the 55 cases in which the abdominal reflex was present, it was markedly exaggerated.

BLADDER REFLEX.

In 115 of the 155 cases, or 74·1 per cent., the bladder reflex was affected in some way or another (forcing, dribbling, retention, incontinence, precipitant urination, &c.); in 29 cases, or 18·7 per cent., the bladder reflex was not affected; and in 11 cases, or 7 per cent., the condition of the the bladder reflex was not specifically mentioned in the notes.

Consequently, in the 144 cases in which the condition of the bladder reflex is specifically mentioned in the notes, urination was affected in 115 cases, or 79·8 per cent., and unaffected in 29 cases, or 20·1 per cent.

In one of the cases in which there was difficulty in urination, the patient was affected with stricture of the urethra. Precipitant urination was only noted in a few cases (Cases 1, 5, 123).

Leimbach noted some derangement of urination in 80·5 per cent. of his cases; Bonar in 62·23 per cent.; Thomas in 65 per cent.; Riley in 70·4 per cent.; and Bramwell in 74·1 per cent

The *vesical crises* are not included in the derangements of urination just considered; they will be dealt with subsequently.

Peculiar sensations attending or following the act of micturition were noted in four cases. In one case, the act of micturition was sometimes followed by a gripping feeling across the chest. In another case, occasionally followed by a severe pain above the pubes; this patient also sometimes felt as if he had a lump in the rectum. In another case, the pressure of making water produced a feeling of irritation and pain in the perineum. rectum, and lower part of the abdomen; and this irritation, the patient said, proceeded in the form of spasms up the body. In another case, the act of micturition was attended with pain in the region of the bladder.

RECTAL REFLEX.

In 98 of the 155 cases, or 63·3 per cent., the rectal reflex was (apparently[1]) affected; in 44 cases, or 28·3 per cent., the rectal reflex was not affected; and in 13, or 8·3 per cent., the condition of the rectal reflex is not specifically mentioned in the notes.

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[1] I say "apparently," for constipation is such a common symptom that in many of these cases the constipation was probably accidental, and not the direct result of the tabes.

Consequently, in the 142 cases in which the condition of the rectal reflex is specifically stated in the notes, it was affected in 98 cases, or 69 per cent., and unaffected in 44 cases, or 30·9 per cent.

SEXUAL REFLEX.

In 73 of the 155 cases, or 47 per cent., the sexual reflex was affected (diminished or completely lost in 72 cases, and exaggerated in one case); in 26 cases, or 16·7 per cent., the sexual reflex was not affected; and in 56 cases, or 36·1 per cent., the condition of the sexual reflex is not specifically mentioned in the notes.

Consequently, in the 99 cases in which the condition of the sexual reflex is specifically mentioned in the notes, it was affected in 73 cases, or 73·7 per cent., and unaffected in 26 cases, or 26·1 per cent.

The only case in which exaggeration of sexual desire or power was noted was Case 24.

In Case 33, the patient stated that after sexual excitement he felt a pain in the perineum, as if he wanted to get the bowels opened; he also complained of a damp cold feeling about the testicles. In two cases, the patients complained of painful erections.

Leimbach found sexual derangement present in 58·25 per cent. of his cases; Bonar in 6 per cent.; Thomas in 58 5 per cent.; Riley in 57·2 per cent.; Bramwell in 47 per cent.

THE RELATIVE CONDITION OF THE CREMASTERIC AND SEXUAL REFLEXES.

In 72 of the 155 cases the condition of both the cremasteric and sexual reflexes was noted.

In 22 of these 72 cases the cremasteric and sexual reflexes were both affected, *i.e.*, the cremasteric reflex was absent (on both sides in 19 and on one side in 3 cases), and the sexual reflex affected (lost or markedly diminished); in 29 of the 72 cases the cremasteric reflex was present (unaffected), and the sexual reflex was affected; in 6 cases the cremasteric reflex was affected (absent)—in five cases on both sides and in one case on one side—and the sexual reflex was unaffected; and in 15 cases both the cremasteric and the sexual reflexes were unaffected.

In 51 cases *in which the sexual reflex was affected* the cremasteric was absent on one or both sides in 22 cases, or 43·1 per cent., and present in 29 cases, or 56·8 per cent.

In Case 24, in which the sexual reflex was enormously exaggerated, the cremasteric reflex was absent.

In 21 cases *in which the sexual reflex was unaffected* the cremasteric reflex was (affected) absent in 6 cases, or 28·5 per cent., and present in 15 cases, or 71·4 per cent.

Consequently, in the 28 cases in which the cremasteric reflex was absent on both sides, the sexual reflex was affected in 22 cases, or 78·5 per cent., and was unaffected in 6 cases, or 21·5 per cent.

And in 44 cases in which the cremasteric reflex was unaffected (present on both sides), the sexual reflex was affected in 29 cases, or 65·9 per cent., and unaffected in 15 cases, or 34 per cent.

These figures show that:—

(1) In those cases of the series in which the sexual function was affected (diminished or lost) the cremasteric reflex was somewhat more frequently present than absent —in the proportion of 56·8 per cent. to 43·1 per cent.

(2) That in those cases in which the sexual reflex is unaffected, the cremasteric reflex is usually unaffected—in the proportion of 71·4 per cent. to 28·5 per cent.

(3) That in cases in which the cremasteric reflex is absent, the sexual function is much more frequently affected than unaffected—in the proportion of 78·5 per cent. to 21·5 per cent.

(4) That in those cases in which the cremasteric reflex is unaffected, the sexual reflex is more frequently affected than unaffected—in the proportion of 65·9 per cent. to 34 per cent.

These results seem to confirm the opinion that, in those cases of tabes in which the cremasteric reflex is affected, the sexual reflex is much more frequently affected than unaffected.

PARALYSIS.

Paralysis, other than ocular paralyses, was present in 16 of the 155 cases, or 10·3 per cent.; absent in 94 cases, or 60·6 per cent.; and not specifically mentioned in the notes in 45 cases, or 29 per cent.

Consequently, in the 110 cases in which the presence or absence of paralysis was specifically mentioned in the notes, it was present in 16 cases, or 14·5 per cent., and absent in 94 cases, or 85·6 per cent.

In eight cases, the paralysis was hemiplegic in distribution; in two of these eight cases the paralysis was merely temporary and apparently functional; in the remaining six cases it was evidently due to organic change, though in most of the cases it was eventually recovered from. In one case the patient had two attacks of hemiplegia: one on the right side (11 years before he came under notice), and the other on the left side (two years before he came under notice). In this case the tabes was of 11 years' duration.

In four cases the paralysis was paraplegic in distribution. In two of these cases it affected the extensor muscles of the legs; in both of these cases the paralysis was recovered from. In two of these cases there was marked muscular atrophy with flaccidity of the muscles of the legs.

In one case, the paralysis was monoplegic in distribution (affecting the arm); in this case the paralysis was temporary.

In one case, there was paralysis of the musculo-spiral nerve.

In one case, facial paralysis (Bell's paralysis) developed during the course of the disease.

In one case, there was some paralysis of the larynx, affecting both the abductors and adductors, and especially the left vocal cord. In this case there was no evidence of thoracic aneurism.

One of the 155 patients had had an attack of poliomyelitis anterior acuta, which had resulted in wasting and shortening of the left leg, in infancy. One patient had, 20 years before coming under notice, a temporary attack of hemiplegia.

One patient complained of a peculiar and alarming feeling of being for some time totally unable to move when waking from sleep. This patient (Case 122) was the subject of laryngeal crises, which often occurred through the night.

In several of the cases in which paralysis occurred, the paralysis was associated with localised muscular atrophy, notably in Cases 26, 85, and 125.

In two cases, the patients made prominent complaint of trembling in the legs. In several cases, the legs were said to give way suddenly when the patient was walking; in some of these cases, the giving way of the legs was associated with sudden lightning pains in the legs; in others not. In six cases, cramps in the legs were complained of. In four cases, the occurrence of flexor spasms is mentioned in the notes. In two cases in which there was no evidence of G. P. I., fibrillary tremors were noted. Choreic-like twitchings were observed in the face, hands, toes, and feet in one case. Peculiar jerking movements in the legs (which were apparently functional) were repeatedly observed in one case, when the patient was sitting with the legs hanging over the side of the bed.

THE CONDITION OF THE PUPILS.

(*a*) *Equality in Size.*—In 54 of the 155 cases, or 34·8 per per cent., the pupils were unequal in size; in 39 cases, or 25·1 per cent., the pupils were equal; and in 62 cases, or 40 per cent., the equality of the pupils is not specifically mentioned in the notes.

Consequently, in 93 cases in which the condition of the pupils as regards their equality is specifically mentioned in the notes, they were unequal in 54 cases, or 58 per cent., and equal in size in 39 cases, or 41·9 per cent.

(*b*) *Size.*—In 69 of the 155 cases, or 44·5 per cent., the pupils were contracted; in 27 cases, or 17·4 per cent., of medium size; in 8 cases, or 5·1 per cent., dilated; and in 51 cases, or 32·9 per cent., the size of the pupils is not specifically mentioned in the notes.

Consequently, in the 104 cases in which the size of the pupils is specifically mentioned in the notes, they were contracted in 69 cases, or 66·3 per cent.; of medium size in 27 cases, or 25·9 per cent.; and dilated in 8 cases, or 7 6 per cent.

Note.—The pupil was measured in a moderate light. Pupils above 5 m.m. in size were classed as dilated; between 5 and 3 m.m. as of medium size; at or below 3 m.m. as contracted. In many of the 69 cases in which the pupils were contracted, they were extremely myotic—1 to 1½ m.m.

Regularity of outlines and margins.—In 16 of the 155 cases, or in 10·3 per cent., the outline of the pupils was regular; in 11 cases, or 7 per cent., the outline of the pupils was irregular; and in 128 cases, or 82·6 per cent., the condition of the pupil in respect to this point is not specifically mentioned in the notes.

Consequently, in the 27 cases in which the condition of the pupils as regards regularity of their margins was noted, they were regular in 16 cases, or 59·2 per cent., and irregular in 11 cases, or 40·6 per cent.

Contractility to light.—In 121 of the 155 cases, or 78 per cent., the pupil reflex to light was completely lost, or very sluggish in one or both eyes; in 24 cases, or 15·4 per cent., the pupils reacted briskly to light; and in 10 cases, or 6·4 per cent., the condition of the light-reflex is not specifically mentioned in the notes.

In 116 cases the pupil reflex to light was completely absent or very sluggish on *both* sides; and in 5 cases was completely absent or very sluggish on *one* side only; in these five cases the pupil reacted briskly to light on the opposite side.

Consequently, when the patient first came under observation, the light reflex was lost or very sluggish in one or both eyes in 121, or 83·4 per cent., of the 145 cases in which the contractility of the pupil was specifically noted, and present in 24 cases, or 16·5 per cent.; and since in four of the 24 cases in which the pupil contracted to light when the patients first came under observation, the light reflex was subsequently lost, the light reflex *was ultimately lost in* 125 *cases*, or 86·1 per cent. of the 145 cases in which the condition of the pupil is specifically mentioned in the notes.

Leimbach found changes in the pupillary reaction in 70·25 per cent. of his cases; Bonar in 78·67 per cent.; Thomas in 72·9 per cent.; Riley in 62·2 per cent.; Bramwell in 80·6 per cent.

Contraction on accommodation.—In 13 cases, or 8·3 per cent., of the 155 cases, the contraction of the pupil on accommodation was either completely absent or very sluggish; in 132 of the 155 cases, or 83·2 per cent., both pupils contracted briskly on accommodation; and in 10 cases, or 6·4 per cent., the activity of the pupil on accommodation is not specifically stated in the notes.

Consequently, in the 145 cases in which the condition of the pupil as regards contractility on accommodation was noted, the contractility of the pupil on accommodation was absent in 13, or 8·9 per cent., and brisk in 132, or 91 per cent.

Leimbach found the contraction of the pupil on accommodation lost in 2 per cent. of his cases; Bonar in 5·2 per cent.; Thomas in 7·2 per cent.; Bramwell in 8 3 per cent.

The Argyll-Robertson condition (*Iridoplegia*).—In 90 cases the complete Argyll-Robertson condition of the pupil (complete loss of the light reflex with active contraction on accommodation) was present on both sides; and in 5 cases on one side; in 13 cases the incomplete Argyll-Robertson condition (sluggish action to light with active contraction on accommodation) was present on one or both sides.

Consequently, when the patients first came under observation, the Argyll-Robertson condition of the pupil was present on one or both sides, in a more or less perfect form, in 108, or 69·6 per cent., of the 155 cases, or in 74·4 per cent. of the 145 cases in which the contractility of the pupil is specifically stated in the notes. But since in four of the cases in which the pupils reacted briskly to light when the patients first came under notice, the Argyll-Robertson condition was subsequently developed, the Argyll-Robertson pupil was ultimately present in 112, or 72·2 per cent., of the total 155 cases, and in 77·2 per cent. of the 145 cases in which the condition of the pupillary reactions is specifically mentioned in the notes.

In 13 of the 155 cases, or 8·3 per cent., or in 8·9 per cent. of the 145 cases in which the condition of the pupillary reaction is specifically mentioned in the notes, the contractility of the pupils both to light and accommodation was lost.

In 24 cases, or 15·4 per cent of the 155 cases, both pupils contracted actively to light and accommodation when the patient first came under observation. In 10 cases, or 6·4 per cent., of the 155 cases, the condition of the pupils as regards contractility is not specifically mentioned in the notes. In four of the 24 cases in which the pupil contracted actively to light when the patient first came under observation, the Argyll-Robertson condition was subsequently developed.

Consequently, the Argyll-Robertson pupil was ultimately present in 112, or 72·2 per cent., of the total 155 cases; and in 77·2 per cent. of the 145 cases in which the condition of the pupillary reaction is specifically stated in the notes.

Leimbach found the Argyll-Robertson pupil, on one or both sides, in a more or less complete form, in 336 cases, or 84 per cent., of his 400 cases; Bonar in 70·6 per cent. of his 286 cases; Thomas in 63 per cent. of his 111 cases; Riley in 62·2 per cent. of his 61 cases; Bramwell in 72·2 per cent.

The condition of the light reflex in 37 *cases in which syphilis was denied.*—It has been suggested that the Argyll-Robertson condition of the pupil is only present in those cases of tabes in which the patients have had syphilis. My cases give no support to this theory.

In 37 cases in which syphilis was definitely denied and in which there was nothing either in the family history or the condition of the patient to suggest previous syphilis, the light reflex was affected in 35, and unaffected only in two cases, and not noted in two cases. In the 33 cases in which the light reflex was affected and in which syphilis was denied, the Argyll-Robertson pupil was present in a complete form in 22 and in an incomplete form in seven. In four cases the pupil contracted neither to light nor on accommodation.

These results are in accord with those of Bonar.[1] He states:—"Schäffer, in his new book on tabes, says that Gowers states that the Argyll-Robertson pupil is only present in those cases of tabes which have had syphilis. I have been unable to verify this reference, but in 20 consecutive cases of those under consideration here which have had syphilis, the Argyll-Robertson pupil was present in each. There is no doubt but that, if this point were investigated in the remainder of the 88 cases in which syphilis was undoubtedly absent, the Argyll-Robertson pupil would be found in many more. At any rate, the fact that the Argyll-Robertson pupil was present in 20 of the 88 cases, in which syphilis was absolutely denied, refutes the statement credited to Gowers."

Optic Atrophy.

This was present in 33 of the 155 cases, or 21·2 per cent.; absent in 109 cases, or 70·3 per cent.; and not specifically mentioned in the notes in 13 cases, or 8·3 per cent. It may, however, be confidently concluded that a marked degree of optic atrophy was certainly absent in these cases.

Consequently, we may conclude that optic atrophy was present in 21·2 per cent., and absent in 78·7 per cent., of the 155 cases observed.

In the 33 cases in which optic atrophy was present, it was much more marked in one eye than in the other in seven cases (Cases 7, 55, 99, 107, 108, 115, and 133), and limited to one eye in three cases (Cases 7, 115, and 133). In one of the cases in which the optic atrophy was unilateral when the patient was first seen, the other eye subsequently became affected.

In seven of the 33 cases the optic atrophy was slight; in seven marked; and in 21 very marked or complete, the patients being almost totally blind, quite blind, or only able to distinguish light from darkness.

In one case (Case 108), double optic neuritis, marked in the left eye and slight in the right, preceded the optic atrophy.

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[1] *Loc. cit.*, p. 265.

In nine cases dimness of vision, due to optic atrophy, was the initial symptom of the disease.

In 25 of the 33 cases in which optic atrophy was present there was ataxia (in three of these 25 cases the ataxia was very slight); and in eight cases no ataxia.

Leimbach found optic atrophy in 6·75 per cent. of his cases; Bonar in 8·74 per cent.; Thomas in 10 per cent.; Riley in 11·4 per cent.; Bramwell in 21·2 per cent.

In regard to the frequency of optic atrophy in different series of cases of tabes, Bonar states:—"Now, if we add together the cases studied by von Gross, Berger, Bernhardt, Leimbach, Thomas, and myself, we have 1,088 cases of tabes, and in 222 of these optic atrophy was present. This gives us a percentage of 20·4 for the occurrence of optic nerve atrophy in those cases. This percentage is rather interesting, as the number of cases is so large, and perhaps comes near the truth of the matter."

INFLUENCE OF THE OPTIC ATROPHY ON THE SYMPTOMS AND COURSE OF THE DISEASE.

In seven of the 33 cases in which there was optic atrophy, the atrophy was so slight that it could not be expected to produce any change in the symptoms or course of the disease. In the remaining 26 cases, in eight cases the development of the optic atrophy seemed to be attended with amelioration of the symptoms and retardation of the tabetic process; in one other case, the pains diminished in severity and frequency after the development of the optic atrophy, but the other symptoms progressed. In one other case in which there were no pains, the patient was for a short time under observation, but no definite statement could be made as to the progress of the disease after the development of the optic atrophy. In 12 cases, the development of the optic atrophy did not produce any amelioration of the symptoms and did not seem to be attended with any retarding effect on the course of the disease. In four cases, the condition of the disease after the development of the optic atrophy is not recorded in the notes.

The fact that in many cases in which optic atrophy is developed in the early stages of tabes—as it usually is—the progress of the disease seems to be retarded or the symptoms ameliorated, is very interesting and remarkable. In many cases it is so striking that some authorities—Dejerine, for example—speak of "*tabes arrested by optic atrophy.*" It will be noted that in nine of my 26 cases in which the optic atrophy was very marked, the development of the optic atrophy coincided with improvement in the symptoms or apparent arrest in the development of the tabetic process, and that in 12 there was no improvement and no arrest. The details of some of the cases, both those in which apparent arrest occurred, and those in which arrest did not occur, are of great interest. But the space which would be demanded for their adequate consideration would be considerable. I propose, therefore, to leave this part of the subject for more detailed consideration in a separate paper.

OTHER OCULAR SYMPTOMS.

Diplopia was noted, as having occurred at some period or other of the case, in 22, or 14·2 per cent., of the 155 cases.

Some form or other of ocular paralysis was noted in 25, or 16·1 per cent., of the 155 cases.

Ptosis in 11 cases, or 7 per cent.; in seven of these cases the ptosis was unilateral, and in four bilateral.

Paralysis of the external rectus in 10 cases, or 6·4 per cent.; on one side in six cases, and on both sides in four cases.

More extensive and complicated paralyses of the external muscles of the eye-ball were present in four cases, or 2·5 per cent.

In one case Case 60), complete paralysis of the 3rd nerve on one side lasted for two years, but was ultimately almost completely recovered from.

In one case (Case 108), double ptosis, more marked in the right eye, with frontal overaction; paralysis of the external recti; paralysis of the right internal rectus.

In one case (Case 111), ptosis of the left eye, slight paralysis of the right external rectus, inability to look upwards with either eye.

In one case (Case 142), paralysis of both external recti and inability to converge with either eye.

Nystagmus.—Nystagmoid jerkings on extreme lateral deviation were noted in four, or 2·5 per cent., of the 155 cases (Cases 35, 39, 43, 45).

Watering of the eyes was complained of in two, or 1·2 per cent., of the 155 cases; and *itching* of the eyes in one case, or ·6 per cent.

CRISES.

Visceral crises of some form or another were present in 24 of the 155 cases, or 15·4 per cent.; absent in 90 cases, or 58 per cent.; and not specifically mentioned in the notes in 41 cases, or 26·4 per cent.

Consequently, in the 114 cases in which the presence or absence of visceral crises was specifically mentioned in the notes, they were present in 24 cases, or 21 per cent.; and absent in 90 cases, or 78·8 per cent.

The nature of these crises was as follows:—(*a*) *Gastric* in 14 cases (Cases 7, 13, 15, 37, 54, 59, 60, 63, 90, 98, 128, 133, 152, 153).

In one other case (Case 51), the patient had suffered for two years from pain and vomiting after dinner, but not after any other meal. These attacks occurred two or three times a week, and did not seem to depend upon the nature of the food taken; the stomach appeared to be perfectly normal. Possibly these attacks were an irregular form of gastric crisis.

In several of the cases in which gastric crises occurred, the vomited matters contained blood; in one case, the condition was for a time thought to be due to ulceration of the stomach.

In three cases, in which the gastric crises were marked, there was no pain in the region of the stomach during the attacks.

In five cases, the gastric crises were the first symptoms of the disease.

(*b*) *Rectal* in three cases (Cases 48, 50, and 81).

In two other cases (Cases 4 and 33), the patients had to go repeatedly to stool (in one case 20 or 30 times) every morning before the bowels were relieved; in both of these cases, the attempts to evacuate the bowel were attended with rectal pain and straining.

(*c*) *Gastric and nasal* in one case (Case 35).

(*d*) *Gastric, rectal, and vesical* in one case (Case 113).

(*e*) *Laryngeal* in three cases (Cases 71, 122, and 127).

In one case (Case 26), attacks of spasmodic difficulty in breathing, which at first sight appeared to be due to laryngeal crises, were found to be due to a small tumour on the left vocal cord.

Laryngeal cough and spasm, probably due to aneurism, was also observed in one case (Case 137).

(*f*) *Intestinal* in one case (Case 58).

(*g*) *Sexual* in one case (Case 24).

In another case (Case 155), the patient was for weeks much troubled with painful erections.

Consequently, *gastric crises* were present, either alone or in combination with other forms of crisis, in 16 cases; *rectal crises*, either alone or in combination with other forms of crisis, in 4 cases; *laryngeal crises*, either alone or in combination with other forms of crisis, in 3 cases; and *vesical, intestinal* (other than rectal), *sexual* and *nasal crises*, either alone or in combination with other forms of crisis, were each present in 1 case.

Of the 16 patients in whom gastric crises occurred (either alone or in combination with other forms of crisis), there were 15 males and 1 female; in the 16 cases, 10 were in the ataxic and 6 in the preataxic stage of the disease. It would, therefore, appear that gastric crises are more apt to be developed in the preataxic than in the ataxic cases, or, at all events, to be developed in the early (preataxic) stage of the disease.

In the four patients in whom rectal crises occurred, either alone or in combination with other forms of crisis, there were two males and two females; all the patients were in the ataxic stage of the disease.

In the three patients in whom laryngeal crises occurred, there were two males and one female; all of these were in the ataxic stage of the disease.

In the case in which sexual crises occurred, the patient —a male—was in the ataxic stage of the disease.

Consequently, in the 24 cases in which crises of one sort or another occurred, there were 20 males and 4 females; and of the 24 cases, 18 were in the ataxic and 6 in the pre-ataxic stage of the disease.

Leimbach observed crises in 5·25 per cent. of his cases; Bonar in 16·78 per cent.; Thomas in 10·8 per cent.; Bramwell in 15·4 per cent.[1]

TROPHIC LESIONS OF BONES AND JOINTS (CHARCOT'S JOINT DISEASE).

Trophic lesions in the bones and joints were present in nine of the 155 cases, or 5·8 per cent.; absent in 131 cases, or 84·5 per cent.; and not specifically mentioned in the notes in 15 cases, or 9·6 per cent.

Consequently, in the 140 cases in which the presence or absence of trophic lesions in the bones and joints is specifically mentioned in the notes, such lesions were present in 9 cases, or 6·4 per cent., and absent in 131 cases, or 93.5 per cent.

The nature of the bone and joint lesions was as follows:—

In one case (Case 29) both knees were affected.

In one case (Case 81) one knee and one thumb were affected.

In one case (Case 139) one knee, hip and thumb were affected.

In one case (Case 106) one knee and both big toes were affected.

In one case (Case 129) one hip and one femur were affected

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[1] I have omitted Riley's figures. In his 61 cases gastric crises occurred 11 times and laryngeal crises 6 times. He has not stated whether the gastric and laryngeal crises occurred in the same or different cases. If one supposes that they occurred in 17 separate cases, then in his 61 cases crises occurred in 27·8 per cent.—a percentage which it is difficult to accept.

In one case (Case 47) one ankle was affected.

In one case (Case 133) the right tibia and fibula (but not the ankle joint) were affected.

In one case (Case 113) the jaw was affected.

In one case (Case 136) the right femur was affected.

Consequently, the *knee* joint was affected alone, or in combination with other joints or bones, in four cases; the *hip* in two cases; the *thumb* in two cases; the *femur* in two cases; and the *ankle*, *toe*, *jaw*, *tibia*, and *fibula* were each affected (either alone or in combination with other joints or bones) in one case.

In one other case (Case 131) the right knee joint became suddenly swollen but not painful. I have not included this case, for when I saw the patient three weeks later, the joint was quite normal.

In three cases the joint affection developed suddenly (in a single night) without apparent cause. In two cases the joint affection seemed to be the result of, or was first noticed immediately after, an injury.

Six of the patients in whom joint or bone lesions developed were males and three were females; in three of the cases the disease developed in the preataxic stage, so far as could be ascertained, in six cases in the ataxic stage of the disease.

In one case the joint affection appeared to be the first symptom of the disease.

Leimbach found trophic changes in the bones and joints in 1·75 per cent. of his cases; Bonar in 2·1 per cent.; Thomas in 5·4 per cent.; Riley in 0 per cent.; Bramwell in 5·8 per cent.

VASOMOTOR AND TROPHIC LESIONS IN THE SKIN AND ITS APPENDAGES.

These were noted in 10 of the 155 cases, or 6·4 per cent. of the 155 cases. Their nature was as follows:—

A herpetic eruption developed at the seat of the lightning pains in four cases. In one of these cases an eruption of herpetic vesicles recurred several times on the sacrum and buttocks after attacks of severe lightning pains in the legs.

I had the opportunity of seeing the eruption; it consisted of a group of herpetic vesicles, covering an area about the size of half-a-crown on the right buttock just outside the natal fold; there were also some cicatrices on the left buttock, the result of previous attacks.

Petechiæ developed at the seat of the pains in two cases.

Extensive ecchymoses occurred in connection with the joint lesions in two cases.

In two cases the *teeth*, which were perfectly sound, *loosened and dropped out* in the course of a few weeks.

A perforating ulcer of the foot developed in one case.

Ulceration of the toes and corns occurred in three cases.

Shedding of the big toe-nails was noted in four cases, but probably occurred in a larger number of cases; in each of these four cases an extravasation of blood occurred beneath the nail before it was shed.

In several cases the toe-nails were very dry, brittle, thickened, and cracked.

In a large number of cases the skin of the soles was dry and much thickened.

MENTAL SYMPTOMS.

In the 16 cases (see page 80) in which symptoms more or less typical of G. P. I. developed, there were of course mental symptoms.

In addition, impairment of memory was noted in five cases; mental depression in four cases; mental irritability in one case.

In the remaining cases of the series, the mental condition was either quite normal or not specifically stated in the notes.

Recurring insanity, not due to the tabes, occurred in one case. In two cases, epileptiform convulsions, for which there was no obvious cause, but which were perhaps the initial symptoms of G. P. I., occurred.

In the great majority of the cases, the mental activity was unimpaired and, indeed, remained so in the later stages of the disease. One patient, for example, for several years after he was confined to bed (with extreme ataxia both of the legs and arms, complete loss of sight in one eye, ocular paralysis, &c.) continued to manage and transact a large business. One patient in the preataxic stage of the disease went through a year's service with his regiment in South Africa and was then invalided home—the exact reason of which I do not know. One patient, a commercial traveller (who was markedly ataxic) transacted a very large business, covering 8,000 miles in the course of his annual journeys.

HEARING.

In 17 of the 155 cases, or 10·9 per cent., hearing was more or less impaired on one or both sides; in 67 cases, or 43·2 per cent., hearing was normal; and in 71, or 45·8 per cent., the condition of hearing was not specifically mentioned in the notes.

I do not attach any great importance to these percentages, for in many of the 17 cases in which hearing was impaired, the impairment was apparently not the direct result of the tabes. The notes are not, however, sufficiently detailed to allow of a definite statement as to the exact cause of the impairment in each case.

In one case, there was persistent tinnitus for two years. In another case, the first symptom was a noise like the singing of a sky-lark in the ear; this persisted until the patient came under observation two years later.

TASTE.

In two of the 155 cases, or 1·29 per cent., taste was lost; in 75 cases, or 48·3 per cent., taste was not affected; and in 78, or 50·3 per cent., the condition of taste was not specifically mentioned in the notes.

SMELL.

In two of the 140 cases, or 1·29 per cent., smell was affected; in 74 cases, or 47·7 per cent., smell was not affected; and in 79, or 50·9 per cent., the condition of smell was not specifically mentioned in the notes.

HEADACHE.

This was complained of in 16 of the 155 cases, or 10·3 per cent.; absent in 70 cases, or 45·1 per cent.; and not specifically mentioned in the notes in 69 cases, or 44·5 per cent.

Consequently, in the 86 cases in which the presence or absence of headache was specifically mentioned in the notes, it was present in 16 cases, or 18·6 per cent., and absent in 70 cases, or 81·3 per cent.

GIDDINESS.

This was present in 13 of the 155 cases, or 8·3 per cent.; absent in 72 cases, or 46·4 per cent.; and not specifically mentioned in the notes in 70 cases, or 45·1 per cent.

Consequently, in the 85 cases in which the presence or absence of giddiness was specifically mentioned in the notes, it was present in 13 cases, or 15·2 per cent., and absent in 72 cases, or 84·7 per cent.

SLEEP.

It was noted that sleep was affected in 30 of the 155 cases, or 19·3 per cent.; unaffected in 69 cases, or 44·5 per cent.; and not specifically mentioned in the notes in 56 cases, or 36·1 per cent.

Consequently, in the 99 cases in which the condition of sleep was specifically stated in the notes, sleep was affected in 30 cases, or 30·3 per cent., and unaffected in 69 cases, or 69·6 per cent.

CONSIDERABLE LOSS OF WEIGHT.

In 59 of the 155 cases, or 38 per cent., there was marked emaciation or considerable loss of weight; in 61 cases, or 39·3 per cent., there was no marked loss of weight; and in 35 cases, or 22·5 per cent., the presence or absence of emaciation and loss of weight is not specifically mentioned in the notes.

Consequently, in the 120 cases in which the presence or absence of emaciation and considerable loss of weight is specifically mentioned in the notes, this condition was present in 59 cases, or 49·1 per cent., and absent in 61 cases, or 50·9 per cent.

In one of the cases in which there was marked loss of weight, the tabes was complicated by phthisis.

In nine cases there was a very considerable increase in weight as the disease progressed (Cases 2, 43, 56, 94, 102, 107, 116, 146, 150).

Riley found considerable loss of weight in 33, or 54 per cent., of his 61 cases.

THE CONDITION OF THE HEART.

In eight of the 155 cases, or 5·1 per cent., some form or another of cardiac lesion was present; in 118 cases, or 76·1 per cent., the heart was normal; and in 29 cases, or 18·7 per cent., the condition of the heart is not specifically mentioned in the notes.

Consequently, in the 126 cases in which the condition of the heart is specifically mentioned in the notes, there was some form of cardiac lesion in eight cases, or 6·3 per cent.; and in 118 cases, or 93·6 per cent., the heart was normal.

The form of lesion in the eight cases in which the heart was affected was as follows:—

Aortic regurgitation in three cases (Cases 32, 56, 77).

Aortic regurgitation, aortic aneurism, and extreme atheroma of the arteries in one case (Case 42).

Mitral regurgitation in three cases (Cases 72, 95, 147).

Aortic and mitral disease in one case (Case 80).

Aneurism of the aorta in one case (Case 104).

In one case (Case 42) an aneurism of the descending thoracic aorta was found *post mortem*; this patient suffered from a fixed, burning pain in the back (under the left scapula), which was difficult to explain during life; his arteries were extremely atheromatous.

A markedly accentuated condition of the aortic second sound, which was thought to be due to a dilated condition of the aortic arch, was noted in four cases (Cases 6, 125, 137, 155).

In one case the action of the heart was extremely feeble, but there was no evidence of any definite disease.

PULSE FREQUENCY.

Riley states that in a considerable proportion of cases of tabes (in 25, or 40·9 per cent., of the 61 cases which he examined) the pulse frequency is increased—85 per minute or above.

With the object of testing this point I have taken 25 consecutive hospital cases, and estimated the average frequency of the pulse during the first 12 days after admission to hospital (in consulting practice where the patient is only seen once or at rare intervals, it is, of course, in many cases, impossible to form any accurate idea of the exact pulse frequency).

In nine of the 25 cases, or 40 per cent., the average pulse frequency was above 85—a percentage which almost exactly corresponds with that of Riley.

The average frequency of the pulse rate in these 25 cases was as follows:—

In these 25 cases, the average morning pulse rate (for the first 12 days after admission was $81\frac{18}{25}$, and the average evening pulse rate for the same period was $81\frac{6}{25}$.

In 15 of the 25 cases, the average morning pulse rate was 85 or below 85 (lowest 63, highest 85); and in 10 cases the average morning pulse rate was above 85 (lowest 86, highest 95).

In 16 of the 25 cases, the average evening pulse rate was below 85 (lowest 61, highest 84), and in nine cases the evening pulse rate was above 85 (lowest 86, highest 93).

In the 14 cases in which both the morning and evening pulse rate was below 85, the morning pulse rate averaged 75, and the evening pulse rate averaged 75.

In the 11 cases in which the pulse rate was above 85, the morning pulse rate averaged 90, and the evening pulse rate averaged 90.

In the 25 cases analysed, the average morning pulse rate was lower than the average evening pulse rate in 12 cases; was higher than the average evening pulse rate in 11 cases; and in the remaining two cases the average morning and evening pulse rates were equal. These results are seen in Table XII.

Table XII.—The Morning and Evening Pulse and Temperature in 25 Cases of Tabes.

No.	No. in Table.	Initials.	In-Patient Case-book.		Pulse.		Temperature.	
			Vol.	p.	Average Morning Frequency.	Average Evening Frequency.	Average Morning.	Average Evening.
1	25	M. H.	2	113	83	72	97·9	98·1
2	26	J. M.	7	1	95	93	97·7	97·9
3	27	M. E.	29	57	82	83	97·2	97·8
4	29	W. N.	63	64	67	71	97·2	98
5	30	G. R.	64	25	65	66	97·1	97·5
6	31	T. C.	65	133	87	90	97·2	97·5
7	32	D. C.	65	85	90	91	97	97·5
8	33	A. G.	66	26	77	80	97·7	98·4
9	35	M. B.	66	59	79	79	97·2	97·6
10	36	C. N.	67	104	94	91	97·1	97·5
11	37	J. T.	67	150	90	84	97·2	97·5
12	38	R. C.	69	20	76	76	97·3	98·2
13	39	W. McD.	72	112	78	82	97·9	98·4
14	40	W. M.	73	85	85	89	97·5*	98*
15	41	J. M.	73	43	77	82	97·4	98·5
16	42	R. G. U.	74	86	89	86	98·2	98·5
17	43	W. J.	75	217	76	73	97·4	97·3
18	44	P. M.	79	92	81	80	97	97·5
19	45	P. M.	77	47	86	88	97·1	97·3
20	46	C. M.	81	72	70	71	97·1	97·4
21	47	D. L.	82	90	93	90	97.1	97·5
22	48	J. M.	86	52	63	61	97·1	97·6
23	122	J. S.	87	1	88	76	98·3	98·1
24	123	W. D.	88	38	88	84	97·6	98·3
25	125	J. R.	86	32	90	93	97·3	98·1

It is possible, I think, that the decrease in the frequency of the pulse which occurred in a considerable proportion of the cases during the evening, is the result of the increased intensity of the pains at this period of the 24 hours; but my observations do not as yet enable me to make any definite statement on this point.

TEMPERATURE.

The average morning and evening temperature in the 25 hospital cases in which the pulse frequency was estimated, has also been estimated during the same period, *i.e.*, the first twelve days after admission (*see Table XII.*).

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* Sudden rise in Temp., due to influenza, 2 days after admission; with this exception, Temp. subnormal both morning and evening.

The average morning temperature in these 25 cases was 97·3 (lowest 97, highest 98·3), and the average evening temperature 97·8 (lowest 97·3, highest 98·5).

In 23 of the 25, the average morning temperature was below the average evening temperature; and in two cases the average morning temperature was higher than the average evening temperature.

Consequently, the increased frequency of the morning pulse rate over the evening pulse rate (which was present in 11 of the 25 cases) was not associated with a corresponding condition of the temperature; in other words, the increased frequency of the morning over the evening temperature rate was not due to the fact that the morning temperature was higher than the evening temperature.

THE CONDITION OF THE URINE.

In seven of the 155 cases, or 4·5 per cent., the urine contained albumen, and in two cases, or 1·2 per cent., considerable quantities of pus; in 117 cases, or 75·5 per cent., the urine was normal; and in 29 cases, or 18·7 per cent., the condition of the urine is not specifically mentioned in the notes.

Consequently, in seven of the 126 cases, or 5·5 per cent., in which the condition of the urine was specifically mentioned in the notes, it contained albumen, and in two cases, or 1·5 per cent., considerable quantities of pus; and in 117 cases, or 92·8 per cent., it was normal.

In two of the five cases (cases 66 and 119), in which the urine contained albumen, the urine contained considerable quantities of pus.

In two of these seven cases in which the urine contained albumen, the amount of albumen was very small; of the five remaining cases, albumen was absent in two cases when the patient first came under observation, and only developed in the later stages of the disease.

COMPLICATIONS.

In addition to the complications and associated lesions enumerated under the foregoing headings, the following were noted :—

General paralysis of the insane.—This developed during the course of the disease in 12 cases; in two other cases, the mental symptoms were suggestive of commencing G. P. I.; in two other cases, cerebral symptoms developed during the last two or three weeks of life which were suggestive of acute G. P. I.

I have not included in this analysis the cases in which tabes dorsalis developed in the course of G. P. I. (these cases are entered in my notebooks as "G. P. I."), but only those cases in which the tabes was the primary disease.

Consequently, in the series of 155 cases of tabes, G. P. I. certainly developed in 12, or 7·7 per cent., and probably in 16, or 10·3 per cent., during the time that the patients have been under observation. And if we take into account the fact that in 49 of the 155 cases, or 31·6 per cent., the progress of the case after the patients came under observation is not known, and also the fact that in 75 cases the disease is still in progress, it may be confidently assumed that general paralysis of the insane developed in this series of 155 cases in a considerably larger percentage than 10·3. This, I need hardly point out, is a very remarkable conclusion.

Pulmonary complications. — Phthisis, in two cases; pleurisy, two cases; bronchitis and emphysema, two cases.

Cardiac and arterial complications.—(See heart and aorta.)

Digestive complications.—Troublesome dyspepsia, one case; dilatation of the stomach, one case; stomatitis (recurring) one case; gallstones, one case.

Urinary complications. — Severe cystitis, three cases; Bright's disease, four cases.

Displacement of the uterus, one case.

Nervous complications.—Recurring insanity, one case; epileptic fits, one case.

Purpura of the legs, one case.

RESULTS.

I have endeavoured to follow out and bring up to date all of the cases. The result of this enquiry is as follows:—31 of the 155 patients have died; 75 are still alive; and in 49 cases the result is not known.

Of the 75 cases which are still alive, 16 are decidedly better than they were a few years ago; the remaining 59 cases are either worse or *in statu quo*.

CAUSES OF DEATH.

The causes of death in the 31 cases which have proved fatal are shown in Table XIII.

Table XIII.—Causes of Death in 31 *Fatal Cases of Tabes.*

G.P.I.	6 cases.
Cerebral symptoms resembling acute G.P.I.	1 case.
Albuminuria and cerebral symptoms resembling acute G P.I.	1 ,,
Apoplexy	3 cases.
Exhaustion and bedsores	2 ,,
Cystitis	1 case.
Phthisis	2 cases.
Influenza and bronchitis	1 case.
Pneumonia	1 ,,
Aneurism (1 ruptured)	2 cases.
Cardiac disease	2 ,,
Atheroma, aortic regurgitation, aortic aneurism, and bedsores	1 case.
Cut throat	1 ,,
Not known	7 cases.
	31

DURATION OF THE FATAL CASES.

The average duration in the 30 fatal cases in which the exact date of death is known was 8·3 years; the longest duration in any of these 30 fatal cases was 22 years, and the shortest duration 1½ years (two cases died 1½ years after the commencement of the disease).

The exact duration in each of the 30 fatal cases in which the exact date of termination is known, is shown in Table XIV.:—

Table XIV.—The total duration of the Disease in 30 Fatal Cases of Tabes:—

Duration.	No. of Cases.
1 to 2 years	2 cases
2 ,, 3 ,,	4 ,,
3 ,, 4 ,,	2 ,,
4 ,, 5 ,,	4 ,,
5 ,, 6 ,,	1 case.
6 ,, 7 ,,	2 cases.
7 ,, 8 ,,	1 case.
8 ,, 9 ,,	2 cases.
9 ,, 10 ,,	3 ,,
	21
Brought forward	21 cases
11 to 12 years	2 ,,
13 ,, 14 ,,	2 ,,
15 ,, 16 ,,	1 case.
16 ,, 17 ,,	1 ,,
19 ,, 20 ,,	1 ,,
20 ,, 21 ,,	1 ,,
21 ,, 22 ,,	1 ,,
Not stated	1 ,,
Total	31 cases

In conclusion, I append a Table (XV.) showing the percentage frequency of the leading symptoms in (1) the total 155 cases under analysis; and (2) the frequency and percentage frequency of the same (the leading symptoms of the disease) in the cases in which the presence or absence of the special symptom under investigation is specifically stated in the notes:—

Table XV.—Frequency and percentage of chief symptoms in 155 cases of Tabes.

Nature of Symptom	Frequency and percentage of different symptoms				
	In total 155 cases.		In those cases in which the symptom was specifically noted.		
	No. of cases in which present.	Per cent	No. of cases in which symptom specifically noted.	No. of such cases in which symptom present.	Per cent.
Lightning pains	148	95·4	155	148	95·4
Pain in the back	45	29	90	45	50
Girdle sensation	67	43·2	98	67	68·2
Paræsthesiæ	103	66·4	118	103	87·2
Numbness	88	56·7	118	88	74·5
Coldness of feet	45	29	118	45	38·1
Pins and needles	20	12·9	118	20	16·9
Ground felt soft	30	19·3	118	30	25·4
Anaesthesia in the legs ..	68	43·8	114	68	59·6
,, ,, arms ..	20	12·9	74	20	27
,, ,, trunk ..	40	25·8	75	40	53·3
,, ,, face ..	2	1·2	58	2	3·4
Analgesia in the legs	55	35·4	91	55	60·3
,, ,, arms ..	40	25·8	72	40	55·5
,, (ulnar)	—	—	60*	29	48·3
Biernacki's sign	—	—	60*	14	23·3
Analgesia in the trunk ..	59	38	78	59	75·6
,, (thoracic)	—	—	60*	45	75
,, in the head .	2	1·2	53	2	3·7
Ataxic gait	120	77·4	155	120	77·4
Rombergism	120	77·4	154	120	77·9
Incoordination in the legs ..	117	75·4	152	117	76·9
,, ,, arms..	39	25·1	108	39	36·1
Muscular sense in the legs ..	67	43·2	97	67	69
,, ,, arms..	24	15·4	76	24	31·5
Muscular analgesia in legs ..	38	24·5	54	38	70·3
Hypotonia in the legs ..	38	24·5	47	38	80·8
Paralysis, other than ocular..	16	10·3	110	16	14·5
Loss of knee-jerks †	127	81·9	147	127	86·3
,, Achillis-jerks	44	28·3	52	44	86·4
,, deep reflexes, upper extremities	23	14·8	45	23	50·9
,, jaw-jerk	7	4·5	39	7	17·9
,, plantar reflex.. ..	19	12·2	116	19	16·3
Exaggeration of plantar reflex	32	10·6	116	32	27·5
Babinski's sign present ..	—	—	47	5	10·6
,, ,, absent ..	—	—	47	39	82·9
No toe movement	—	—	47	3	6·3
Loss of cremasteric reflex ..	30	19·3	85	30	35·2
Derangement of bladder reflex	115	74·1	144	115	79·8
,, rectal ,,	98	63·8	142	98	69
,, sexual ,,	73	47	99	73	73·7

* The last 60 cases of the series specially examined.

† When the patient first came under observation; ultimately lost in 132 cases, or 89·7 per cent. of the 145 cases in which examined.

Nature of Symptom.	Frequency and percentage of different symptoms				
	In total 155 cases.		In those cases in which the symptom was specifically noted.		
	No of cases in which present.	Per cent.	No. of cases in which symptom specifically noted.	No. of such cases in which symptom present.	Per cent.
Pupils:—					
Inequality in size	54	34·8	93	54	58
Myotic	69	44·5	104	69	66·3
Medium	27	17·4	104	27	25·9
Dilated	8	5·1	104	8	7·6
Irregularity of margins ..	11	7	27	11	40 6
Loss of light reflex	125	80·6	145	125	86·1
Loss of cont. on acc. ..	13	8·3	145	13	8·9
Argyll-Robertson pupil ..	112	72·2	145	112	77·2
Optic atrophy	33	21·2	155	33	21·2
Diplopia	22	14·2	—	—	—
Ocular paralysis	25	16·1	—	—	—
Nystagmus	4	2 5	—	—	—
Watering of the eyes	2	1·2	—	—	—
Itching of the eyes	1	·6	—	—	—
Crises	24	15·4	114	24	21
Gastric ‡	16	10·3	114	16	14
Rectal ‡	4	2·5	114	4	3·5
Laryngeal ‡	3	1·9	114	3	2·6
Vesical ‡	1	·6	114	1	·8
Intestinal ‡	1	·6	114	1	·8
Sexual ‡	1	·6	114	1	·8
Nasal ‡	1	·6	114	1	·8
Trophic lesions in bones and joints	9	5·8	140	9	6·4
Trophic lesions—skin and its appendages	10	6·4	—	—	—
Mental symptoms	10	6·4	155	10	6·4
G.P.I. §	12	7·7	155	12	7·7
Headache	16	10·3	86	16	18 6
Giddiness	13	8·3	85	13	15·2
Derangement of sleep ..	30	19·3	99	30	30·3
Impairment of hearing ‖ ..	17	10·9	—	—	—
,, taste	2	1·29	—	—	—
,, smell	2	1·29	—	—	—
Considerable loss of weight ..	59	38	120	59	49·1
Cardiac disease	8	5·1	126	8	6·3
Albuminuria	7	4·5	126	7	5·5

‡ Either alone or in combination with other forms of crisis.

§ In four other cases symptoms suggestive of G.P.I. developed; consequently, G.P.I. was probably present in at least 10·3 per cent. (see p. 80).

‖ In many of these cases the loss of hearing was not directly due to the tabes.

A CASE OF CONGENITAL SPINAL MUSCULAR ATROPHY (FAMILY TYPE), AND A CASE OF HÆMORRHAGE INTO THE SPINAL CORD AT BIRTH, GIVING SIMILAR SYMPTOMS.

BY C. E. BEEVOR, M.D., F.R.C.P.

Physician to the National Hospital, Queen Square, and the Great Northern Hospital.

THE two infants, a boy and a girl, were admitted into the National Hospital, Queen Square, under my care, within a few weeks of each other, and they presented at birth almost identical symptoms of complete paralysis of all the muscles of the lower limbs and trunk, excepting the diaphragm; in the first case there was also complete paralysis of both arms, and in the second, partial paralysis of one arm. In both cases all the affected muscles were flaccid and did not react to faradism, and there was loss of sensation in the legs and trunk as high as the 2nd dorsal segment.

The symptoms in the first case were due to a progressive atrophy of the cells of the anterior horns and degeneration of the posterior columns which had commenced in utero, and in the other to hæmorrhage into the spinal cord caused by dislocation of the spinal column at birth, and to stretching of the right brachial plexus. The notes of the two cases were taken by Dr. James Collier, the House Physician at the National Hospital.

Case 1.—William J. G——, 5 weeks old, was admitted into the National Hospital, Queen Square, on February 6, 1899.

Family History was good, and there was no history of fits, insanity, nervous diseases in the family (excepting the other brothers and sisters), and no rheumatism or consumption. The mother's father had gout, and her mother had hemiplegia.

The mother has been married seventeen years, and has had eight children. The first was a girl, full term, easy birth, vertex presentation. At the end of a month it was noticed to be paralysed all over like the present case, but not so severely in the neck. It was taken to St. Thomas' Hospital, and at four months old to Great Ormond Street Hospital, under the care of Dr. Barlow and Dr. Angel Money. It died at home at 4½ months; no autopsy. Second child was a girl, and born naturally, and it moved all its limbs at first. At six months old it became ill, and then gradually it became weak all over. It was taken to Great Ormond Street Hospital, under Dr. Money. It died at eight months old, and at the autopsy the brain was said to be healthy, but the spinal cord was not examined. Third child was a boy, and was all right and well at 14 years. Fourth child, full term, weighed 11 lbs., was all right at birth, but at six weeks old it became paralysed gradually, first in the left arm, then the right arm, then the left leg, and lastly the right leg. It went to Great Ormond Street, under Dr. Money. It died at seven months, and Dr. Money removed the brain and spinal cord, but with what result is not known. Fifth child, all right, aged 9 years. Sixth child, full term, weighed 9½ lbs., all right, aged 8 years. Seventh child, full term, all right, aged 1 year and nine months. Eighth child is the patient.

History of Case.—The patient was a full-term child and weighed 15 lbs. at birth. The presentation was vertex, with difficult labour, especially in the delivery of the shoulders. The child was black all over when born from asphyxia, and was at once noticed to be paralysed. The mother stated that she had never felt the child move in utero. The child was said to have moved the left hand less well subsequently.

Present State.—On admission the child was well developed and well nourished. It looked quite healthy and seemed well, and took its food, and was lively and contented. As it lay in bed there was seen to be absolute paralysis of the intercostal muscles, and all four limbs were flaccid and motionless, with the exception of slight movements of the fingers of the left hand.

Special Senses.—The vision was acute; there was no hemianopia. The optic discs were healthy.

Cranial nerves were all healthy, as far as they could be examined, and there were no bulbar symptoms. The child was able to suck powerfully.

Trunk Muscles.—There was complete paralysis of all the muscles of the trunk, including the intercostals, except the diaphragm, which acted powerfully. With each inspiration the thorax was drawn down and compressed, and the intercostal spaces were drawn inwards. The neck was very weak, and the head fell about and was not supported by the muscles of the neck. The sterno-mastoids did not act in inspiration, but the upper part of the trapezius was seen to take part in this movement.

Limbs.—There was absolute flaccid paralysis of all the four limbs, with the exception of the very slight involuntary movements of the left fingers, which were continually taking place.

Electrical Reactions.—The faradic excitability of all the muscles of the four limbs, and of the muscles of the trunk, was completely lost, but to the constant current these muscles reacted slowly, and gave A C C > K C C—the reaction of degeneration. The muscles of the face reacted normally to both currents, but the the sterno-mastoids reacted feebly to the faradic.

Sensation to all forms of stimulation was lost in the lower limbs, in the trunk, as high as the second rib, and also in both the upper limbs, including the area over the shoulders supplied by the fourth cervical roots. Tactile sensibility was difficult to prove for certain, but while algesic stimulation produced no effect below the level of the second rib, as soon as this was passed the child gave evidence that it felt above this level.

Sphincters.—Reflex action of the bladder was performed normally, and the anus was not patulous.

Reflexes.—Plantar present, with a slight extensor response; abdominal absent; cremasteric present and brisk; knee-, wrist- and elbow-jerks absent. Other organs normal.

Cranium and *spine* were normal.

On February 14 slow athetoid movements were continually seen in the left fingers and in the toes of both feet. The superficial reflexes were still present.

On February 25 there was more movement in the left hand and arm. The lower extremities were wasting rapidly.

On February 27 the child became cyanosed, and very little air entered the lungs. There was great inspiratory retraction of the whole thorax, but if the lower ribs were held forcibly up by placing the tips of the fingers below them and pulling upwards, so as to fix the thorax, the cyanosis disappeared.

On February 28 the child died, after living eight weeks.

For the account of the *post-mortem* examination in the two cases I am much indebted to Dr. Batten, who was then Pathologist to the Hospital.

PATHOLOGICAL EXAMINATION BY DR. F. BATTEN, F.R.C.P.

Method of Examination.

Both the following cases were examined by the same methods, and the same reagents were used in hardening.

All the tissues examined were hardened in 10 per cent. formalin. After three or more days portions of the cerebrum, cerebellum, pons, medulla, and cord were removed and placed into absolute alcohol for examination of the cells by the Nissl method. Other portions of the same tissues, together with portions of the nerves and muscles, were placed into Marchi's fluid, and other portions into concentrated Muller's fluid. All these tissues, after washing and dehydration, were embedded in celloidin and cut. Those tissues stained by Marchi's method were at once mounted in xylol canada balsam, and the remainder were further stained by the Weigert-Pal, v. Giesson and Stroebe methods.

Post-mortem Examination.

Case 1.—W. G., aged 8 weeks.

The body was well nourished, although the limbs were somewhat wasted and flaccid. There was some bronchopneumonia, but otherwise the thoracic and abdominal viscera appeared normal.

The cerebrum, cerebellum, pons and medulla appeared natural, and nothing abnormal could be seen in the spinal cord or spinal column. (Plate IV., Fig. 2.)

The roots of the right brachial plexus were embedded in a mass of connective tissue, forming with the surrounding tissue a hard mass.

Microscopical Examination.

Nothing abnormal could be found in the cerebrum or cerebellum, either by the Nissl, Weigert-Pal, or Marchi methods.

The cells of the cranial nuclei stained fairly well, and those of the 12th nucleus very well. It is certain that there was no marked change.

The most striking changes were seen when various segments of the spinal cord were examined. In a section taken at the level of the 4th cervical segment, four normal cells could be seen in the anterior horn of one side. These cells measured ·04mm. in diameter, their chromophilic substance was well stained, there was a distinct nucleus and nucleolus, and the prolongations of the cells were well seen. Near to these normal cells was seen one large swollen cell, with the chromophilic substance peripherally situated, and an indistinct groundwork nucleus and nucleolus; the remaining cells that could be seen were small and atrophied, measuring less than ·02mm. (Plate I., fig. 1); while the normal cells in this region measure ·04. (Plate I., fig. 2.) In these cells there was very little chromophilic substance left; no cell processes could be seen, and in addition to the atrophy of the cells it was obvious that they were greatly diminished in number.

There was no evidence of any vascular engorgment, nor was there any small cell infiltration in the neighbourhood of the degenerate cells.

All the other cervical levels at which the cord was examined, viz., 2nd, 3rd, 5th, 7th, showed exactly the same features; and the 4th cervical segment has been described because it contained more normal cells than any of the other segments; for instance, only one normal cell could be found at the level of the 7th cervical, and none at the other levels. (Plate I., fig. 1.)

In the thoracic region exactly the same features were visible, and the cells have undergone marked atrophy; but in contrast to the atrophy of the cells of the anterior horn the cells of Clarke's column were well formed and stained in their normal manner.

In the lumbar region the atrophy of the anterior horn cells was even more striking owing to their comparatively large size in the normal cord.

The cells in this region measured less than ·03mm., while the cells of the normal cord measure from ·04-·05mm. (Plate I., figs. 3 and 4.)

Passing then to the examination of the spinal cord by

FIG. 1.—Cells of the anterior horn at the level of the 7th cervical segment stained by Nissl's method—from case of progressive muscular atrophy in an infant.

The cells are seen to be extremely small when compared with the normal—measuring about ·02 mm. in diameter, while the normal (fig. 2) measures about ·04 mm. The nucleus and nucleolus are seen distinctly but do not occupy a central position. Some fine granules can be seen in the cells but they are much finer and smaller than the normal chromophilic substance—the cell processes are wanting.

FIG. 2.—Cells of the anterior horn at the level of the 3rd cervical segment, from the case of birth injury to the spinal cord. Stained by Nissl's method.

The cells are well formed, having a normally placed nucleus and nucleolus. Its chromophilic granules are normal and the cell processes are well seen.

The cells are normal and are here given for the purpose of comparison with fig. 1—the two children being nearly of the same age.

FIG. 3.—Cells of the anterior horn at the level of the 2nd lumbar segment from the case of progressive muscular atrophy in an infant. Stained by Nissl's method.

The cells are seen to be extremely atrophied when compared with the normal (fig. 4).

The nucleus and nucleolus are about the normal size and in some cases seem to occupy the whole cell. The normal chromophilic substance has for the most part disappeared and the staining of the cells is very defective.

FIG. 4.—Cells of the anterior horn from the lumbar region of the cord of young child—showing the normal condition of the cells—stained by Nissl's method.

The cells are rather larger than the normal cells of the cervical region, they have a well-marked nucleus and nucleolus, distinct chromophilic substance and long cell processes.

PLATE I.

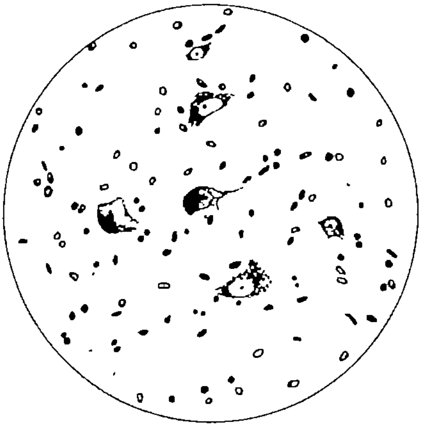

Fig. 1

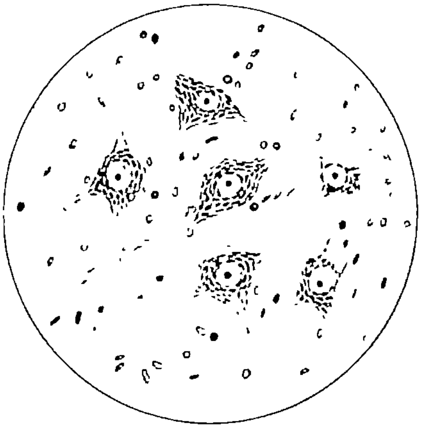

Fig 2.

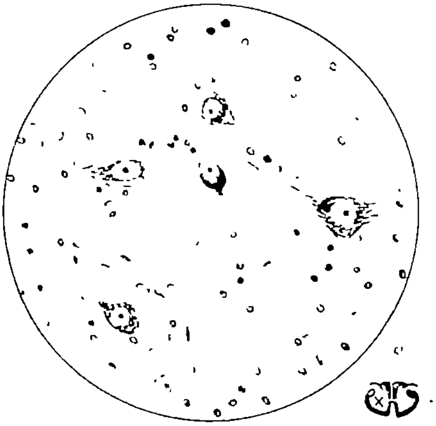

Fig. 3.

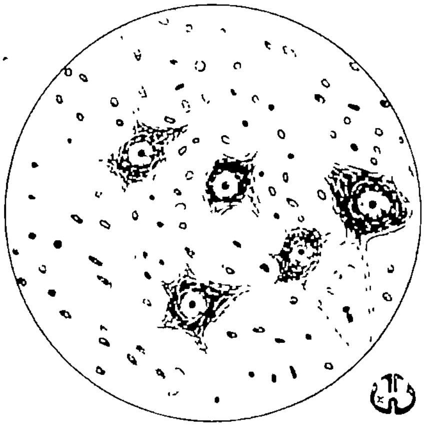

Fig. 4.

the Marchi method, degenerate fibres were found throughout the posterior columns. In the lumbar regions these fibres were situated in the position indicated in Plate II., fig. 11; in the thoracic region they were situated in a more ventral position (figs. 9 and 10); while in the lower cervical region they were distributed evenly throughout both tracts. At the level of the 5th cervical (fig. 7), however, a very marked accession of degenerate fibres could be seen entering and situated in the root zone. These fibres could be traced up into the funiculus cuneatus of the same side. Scattered throughout both the funiculus gracilis and funiculus cuneatus were numerous degenerate fibres. No other degenerate fibres could be seen within the cord. (Plate II., figs. 1-11.)

In spite of this degeneration in the posterior columns, no degeneration could be shown to be present in the posterior nerve roots by the Marchi method.

The degeneration which was present in the lumbar and thoracic region of the cord was insufficient to be observable by the Weigert-Pal method, but the degeneration which was present at the level of the 5th cervical root was obvious by this method, and could be traced upwards to the funiculus cuneatus. By this method the crossed pyramidal tracts appeared paler than the direct cerebellar tracts which were in immediate contact with them; but this cannot be considered as a pathological condition, for it is commonly present in the cords of young children.

The cells of the posterior root ganglia appeared normal.

Nerves.—Several of the peripheral nerves were examined both in longitudinal and transverse section. The right and left vagus, the right and left phrenic, the right and left median, and the right and left anterior crural were found to be normal. Degenerate fibres were present in both brachial plexuses. These were more numerous in the right than the left.

Muscles.—On examination of the fibres of the right biceps muscle it was found that they were considerably atrophied, measuring about ·008-·012mm. in diameter, while the normal fibres of a child 7 weeks old measure about

Series of sections from case W. G. stained by the Marchi method. The drawing has been made under an Edinger projection apparatus.

In fig. 11, a section from the lumbar region, a few degenerate fibres are to be seen in the posterior columns. The same condition is seen in the dorsal and lower cervical regions (figs. 10, 9, 8.)

At the level of the 5th cervical (fig. 8) there is a distinct accession to the degenerate fibres on the right side, and this degeneration can be traced upward through the upper cervical segments (figs. 6, 5, 4) into the medulla, where the greatest number of degenerate fibres occupy the funiculus cuneatus (figs. 3 and 2), though there are degenerate fibres scattered throughout both the funiculus gracilis and the funiculus cuneatus of the opposite side.

PLATE II.

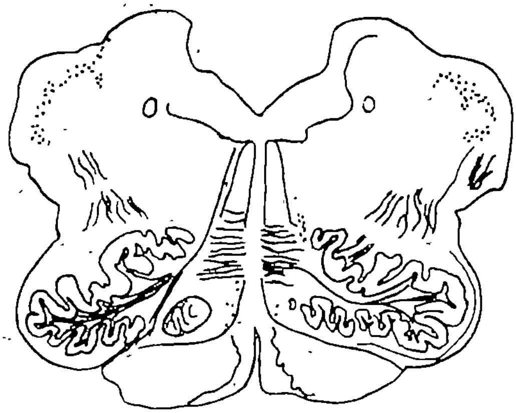

Fig. 1.

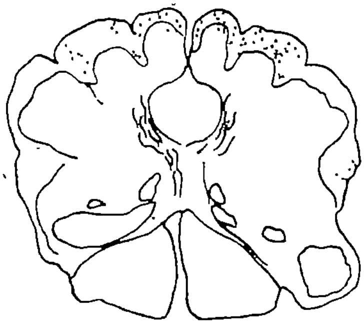

Fig. 2.

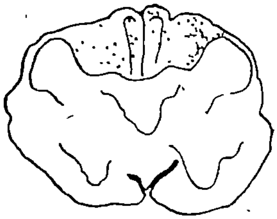

Fig. 3.

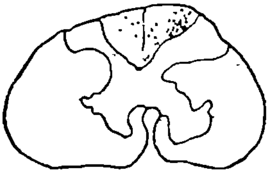

Fig. 4.

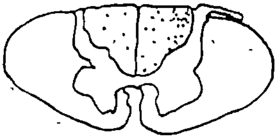

Fig. 5.

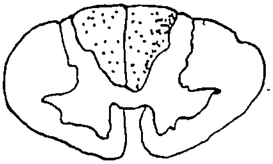

Fig. 6.

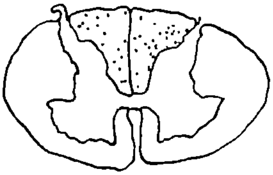

Fig. 7.

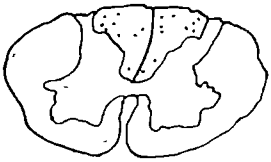

Fig. 8.

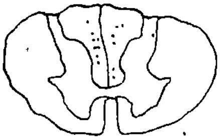

Fig. 9.

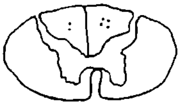

Fig. 10.

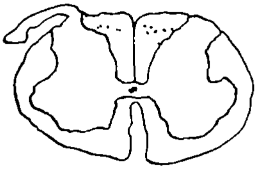

Fig 11.

.02mm. in diameter. (Plate III., figs. 1 and 2.) The transverse striation was well preserved, and no fatty change could be seen. Very few intermuscular medullated nerve-fibres could be seen. The muscle-spindles were well preserved and the intrafusal muscle-fibres were of normal size—*i.e.*, ·02mm. The nerve passing to the spindles appeared normal.

On examination of the left biceps, however (Plate III., fig. 3), a very marked variation in the size of the muscle-fibres was seen; some of the fibres measured ·03mm. in diameter, while others were so atrophied as to measure less than ·004mm. The striation of the fibres was well preserved. In contrast with the condition seen in the right biceps, there were within the muscle numerous nerve-fibres. The spindles were normal, and the nerves passing to them were well stained.

Such a condition cannot but suggest that hypertrophy of muscle-fibres is a compensatory process, for in the muscle in which the nerve-fibres were practically absent the muscle-fibres were simply atrophied, while in the muscle in which only a portion of the nerve had been damaged, there was considerable hypertrophy of some fibres and atrophy of others.

The left rectus femoris was composed of fibres of most varying size; some bundles had fibres of normal size, while the neighbouring fibres were small and atrophied. The large fibres measured about ·024 mm. and the smaller ones ·004 or less. The muscle-spindles were normal, and there were fairly numerous nerve-fibres between the muscle-fibres.

The same description would apply to the right rectus femoris. The transverse striation was well preserved.

Summary.—The changes found were as follows:—

(1) Atrophy of the cells of the anterior horn throughout the spinal cord.

(2) Degeneration in the posterior columns of the spinal cord from the lumbar to the cervical region.

(3) Degeneration of the 5th right cervical root within the spinal cord, this degeneration being traceable to the funiculus cuneatus.

(4) Hypertrophy and atrophy of muscle-fibres.

PLATE III.

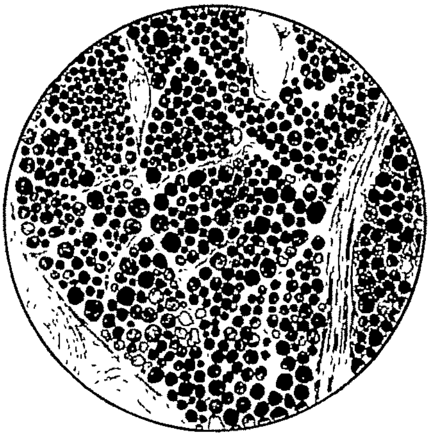

FIG. 1.—Transverse section of the right biceps muscle of child (aged 8 weeks) with progressive muscular atrophy (case 1), stained with Marchi fluid.

The muscle fibres are seen to be of various sizes, some are normal, others have become atrophied to a very marked degree.

It is to be noted that very few nerve-fibres could be found between the muscle-fibres in this muscle. Compare with plate ii, fig. 3

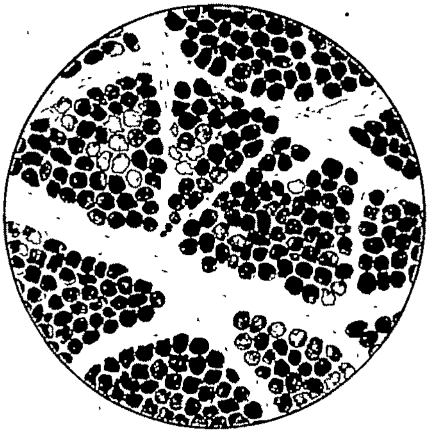

FIG 2.—Transverse section of normal biceps muscle from a child aged 7 weeks. Stained by Marchi's fluid.

The muscle fibres are seen to be of nearly uniform size, measuring between ·01 to ·02 mm. in diameter.

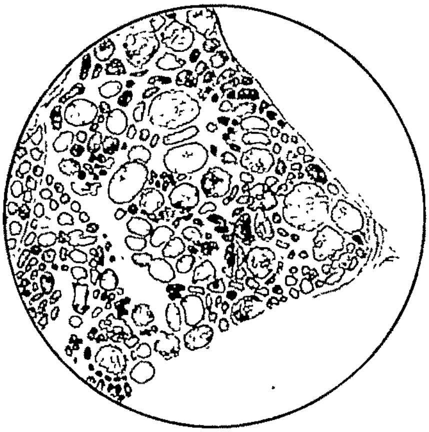

FIG 3.—Transverse section of the left biceps muscle of child (case 1, aged 8 weeks), with progressive muscular atrophy, and stained by Marchi fluid.

The muscle-fibres are seen to be of most various sizes—some appear to have 2 to 3 times the normal diameter, while others are atrophied so as to measure less than ·004 mm. The largest fibre measures over ·03 mm. in diameter.

It is to be noted that there are many more normal nerve-fibres in this muscle than could be found in the corresponding muscle on the right.

(5) Destruction of some roots of the brachial plexus, the right being more affected than the left.

In this case we have a child, who is noticed at birth to be paralysed in all its limbs, in all the trunk muscles with the exception of the diaphragm, and, to a less degree, in the neck muscles ; so that all the muscles except the diaphragm, the face muscles, and others supplied by the cranial nerves, were involved. All the affected muscles were very much wasted, and another extraordinary condition was that not a single one of the paralysed muscles gave any reaction to the faradic current, though they gave the reaction of degeneration with the constant current. Another curious symptom was that there was analgesia, and probably also anæsthesia, of the whole trunk and of all the limbs. It was very difficult in an infant so young as this to be sure where the line of loss of sensation on the trunk ceased, but the child showed marked signs of algesia when the level of the 2nd rib was passed, while it gave no indication of feeling any form of sensation in the trunk below this level. The knee-jerk, as might be expected, was lost, but the plantar reflex was present, and the cremasteric was also very well marked. With so much wasting of muscles one was hardly prepared to find the vesical reflex action performed naturally, and the tonus of the sphincter ani to be maintained.

One of the most important points of this case is the family history. Out of eight children three other girls were affected like the present case, but with the difference that they were born apparently healthy, and at the end of a month or six weeks they became weak all over—in one case the arms preceding the legs—with wasting of muscles.

On looking at the pathological changes found after death, the complete paralysis of movement and the wasting of all the muscles of the limbs and trunk, except the diaphragm, and the complete absence of faradic excitability, would be explained by the extensive atrophy of the cells of the anterior horns throughout the spinal cord, while the escape of the diaphragm would be accounted for by the observation that more normal cells were found at the 4th cervical level than in the other segments. The change in the cells was that which is found in progressive muscular atrophy, and most of them were small, and measured half the natural size, and they had lost the cell processes and possessed very little chromophilic substance. There was, however, no vascular engorgement and not any small-cell infiltration near the cells, such as might have been produced by a myelitis. As the cells were diminished in number it is probable that many of them must have disappeared altogether, but it is also possible that some of them had never been formed.

The loss of sensation in the trunk up to the level of the 2nd rib and in the limbs would be explained by the degenerate fibres in the posterior columns of the cord, shown by the Marchi method, but it is remarkable that no degeneration could be shown in the cells of the posterior root ganglia or in the posterior nerve roots. It is also curious that no degeneration was found in the median or anterior crural nerves. Degenerate fibres were found in both brachial plexuses, and especially on the right side, on which side also the brachial plexus was seen to be imbedded in a mass of connective tissue. It seems highly probable that this was caused by traction on the arms at birth producing rupture of the right brachial plexus, the result of the difficulty in delivering the shoulders, and was a separate lesion from the principal pathological conditions, which were alone quite sufficient to cause atrophy and paralysis of the arms.

The absence of the knee-jerks and wrist-taps would be caused by the atrophy of the anterior cornual cells, but with this extensive atrophy one hardly expected to have the plantar reflex present and to have the cremasteric reflex active.

In connection with this last it is instructive to note that the sphincters were normal, and the anus was not open. As in progressive muscular atrophy in the adult the sphincters escape when the muscles of the limbs and trunk are extensively atrophied, it seems probable that the cells which preside over the sphincters and the cremasteric reflex are either the last to be attacked in progressive muscular atrophy, or that they are situated elsewhere than in the anterior horns, and perhaps in the cells of Clarke's columns, which were here normal.

It is rather difficult to understand why the motor and sensory symptoms should have been so much more severe below the level of the 4th cervical, as there was hardly sufficient change in the condition of the spinal cord above and below this point to allow of this difference, although it is noted that at the level of the 4th cervical the cells were more numerous.

On looking up the literature on the subject of muscular atrophy occurring in children, this case most resembles a class of cases described by Werdnig,[1] Hoffmann,[2] and one by Thomson and Bruce.[3]

In all these cases[4] described by Werdnig and by Hoffmann there was a strong hereditary history, and several members of the same family were attacked. The disease began between the ages of 7 and 10 months, and the muscles which were first affected were those of the hips and back, and later the shoulders, the thighs, the upper arm, forearm, the leg, and lastly the muscles of the hands and feet. Fibrillar twitchings occurred, and though the limbs were usually flaccid, contractions of the hips and knees were discovered in Werdnig's first case, and also of the calf muscles in other cases. The muscles wasted very much, and they lost their faradic excitability, and gave the reaction of degeneration with the galvanic current. The deep reflexes were lost, but the sphincters were normal as a rule, though in one case they were affected. Sensation appeared to be normal in all the cases, and there was no pain and no tenderness. These cases died at the end of a few months or years, varying from fourteen months to six years old, from bronchitis.

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[1] WERDNIG. "Zwei Frühinfantile Hereditare Fälle von Progressiver Muskelatrophie unter dem Bilde der Dystrophie, aber auf Neurotischer Grundlage."—*Archiv. fur Psychiatrie*, 1891. *Ibid:* "Die Fruhinfantile Progressive spinale Amyatrophie."—*Archiv. fur Psychiatrie*, 1894.

[2] HOFFMANN. "Ueber Chronische spinal Muskelatrophie in Kindesalter auf familiärer Basis"—*Deutsche Zeitschrift fur Nervenheilkunde*, 1898. *Ibid:* "Weiterer Beitrag zur Lehre von der Hereditären Progressiven Spinaten Muskelatrophie in Kindesalter."—*Deutsche Zeitschrift fur Nervenheilkunde*, 1897. *Ibid:* "Ueber die hereditare progressive Spinale Muskelatrophie im Kindesalter."—*Munich. Med. Wodschr.*, xlvii., 48, 1900.

[3] THOMSON AND BRUCE. "A Case of Progressive Muscular Atrophy in a child with a Spinal Lesion."—*Edinburgh Hospital Reports*, 1893.

[4] See abstract of these cases by Dr. F. E. Batten, BRAIN, No. 80, vol. xx.

Thomson and Bruce's case differed slightly from the foregoing ones, as the disease began in the second year and the child died at six years old, and there was more pain, but otherwise the muscles attacked were much the same.

Out of the eight cases described by these authors, five were examined after death, and in all of them the chief lesion was atrophy of the cells of the anterior cornua of the spinal cord, with degenerative changes in the anterior roots and the peripheral nerves, and in some cases some degeneration in the pyramidal tracts, but with no changes in the posterior cornua or the posterior columns.

The case which is described in this paper, though it has several points in common with the above recorded cases, differs from them in many respects. It agrees with them in the hereditary predisposition of several members of one family to be attacked, and also in the list of the muscles which were involved, and in their behaviour to electrical testing—although in my case the paralysis and wasting appear to have been more intense—also in the absence of the knee-jerks and the normal condition of the sphincters.

The case here described differs entirely from the foregoing cases in that sensation—especially analgesia—was entirely abolished up to the level of the 2nd rib, and also in the age at which the symptoms began. In the three other children of this family who were similarly affected, the symptoms began at the ages of four to six weeks, and the children died within four to eight months, while in the present case the symptoms began *in utero*, and the child died when nine weeks old, so that the disease in this family began earlier, and was very much more rapid, than in the recorded cases.

Pathologically the present case agrees with the recorded cases in that the cells of the anterior cornua were extremely atrophied, but it differs from them in that the posterior columns were degenerated, which would account for the loss of sensation—a symptom not observed in the recorded cases.

Haushalter[1] described a case of a girl who, in the first months of her life, gradually lost power in the limbs, and six months after had difficulty in carrying her hand to the mouth. The abdominal wall muscles did not contract. She was paralysed in the lower limbs, and was weak in the upper limbs.

Bruns[2] described three cases. The first case was a girl, whose two brothers had also died from the same disease, and the other two cases, a girl and a boy, were sporadic cases. These cases agreed with those of Werdnig and Hoffmann in all particulars, except the duration, as the first case lived till 16, the second is now 12 years old, and the third case is 6. In the first and third cases the disease started after the second year when they could walk.

The case described in this paper differs very much from the cases of progressive muscular atrophy occurring in the adult, and also those which occur in children. The rapidity with which the symptoms came on and caused death in three to six months in the cases of the sisters of this patient, and although I have no record of any loss of sensation in these other children, the loss of sensation was quite definite in my patient. As in this case there was no evidence of inflammation, and as the cells of the anterior horns had the same appearance as is found in progressive muscular atrophy, and we must look upon this case as a hereditary progressive muscular atrophy, beginning in utero, but differing from other cases which have been described in having degeneration in the posterior columns, producing loss of sensation over the trunk and all the limbs. As loss of sensation is not found in progressive muscular atrophy, either in the adult or in children, this case seems to belong to a different type.

A case which most resembles my case is one by M. Sevestre,[3] where a child of 2½ months old was paralysed in the whole body with the exception of the muscles of the head and neck and the diaphragm, which showed normal movements. The muscles of the extremities were atrophic, the faradic excitability was absent, while the galvanic gave a preponderating anodal contraction. The thorax was deformed, and the child had fits. There was also in this case a hereditary history, in that of five sisters two had similar symptoms of paralysis, and both died from an affection of the lungs. There was no mention of a *post mortem* in any of the cases. Here the hereditary history, the distribution of the paralysis, and the loss of the faradic excitability were a counterpart of my case, but there was no mention of any loss of sensation.

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[1] HAUSHALTER, P. "Trois nouveaux cas d'Amyotrophie primitive progressive dans l'enfance."—*Revue de Medicine*, *No.* 18, 1898.

[2] BRUNS. "Zur Casuistik der infantilen progressiven spinalen Muskelatrophie von familialem, resp. hereditärem Charakter."—*Deutsche Ztschr. f. Nervenhkde.*, xix. 5 u. 6, p. 401, 1901.

[3] SEVESTRE "Paralysie flasque des quatre membres et des muscles du tronc (sauf le diaphragme) chez un enfant de deux mois et demi."—*Bulletins de la Société de pediatrie de Paris*, 1899, No. 1-2. (Abstracted in the *Neurologisches Centralblatt*, 1900, No. 19.)

The second of my cases is brought forward, as it was admitted a few weeks before the case just described, and presented almost identical symptoms; it forms, therefore, a very good comparison with the other case.

Helen E. W——, aged 6 weeks, was admitted to the National Hospital, Queen Square, under my care, on January 16, 1899.

From the notes which were taken by Dr. Collier, it appeared that the mother considered the child to be suffering from paralysis of the right arm and of both the legs.

Family history was good. There were four other children in the family, all healthy. There was no history of fits, insanity, or of any nervous disease. There was no gout or rheumatism,

The history of the case was that it was a full-term child, but that the labour was difficult, with a foot presentation, and lasted twelve hours.

Directly after birth both the legs were noticed to be flaccid and paralysed, and the right arm was seen to be paralysed and twisted. Since birth the child has been noticed to move the right arm, but not the legs. There have been no convulsions, and otherwise the child has seemed in good health.

On Admission.—The child, which was sparsely nourished, did not seem to be in any pain, and did not cry much.

On examining the special senses, as far as was possible, it was found that the vision was acute, and there was no hemianopia. The optic discs were normal. The cranium and spine appeared normal.

Cranial Nerves.—Pupils were rather small, and reacted to light. All the cranial nerves so far as they could be tested were normal. There was no nystagmus.

Trunk Muscles.—The diaphragm moved freely, but there was absolutely no intercostal movement. Though the sterno-mastoids, trapezii, and scaleni acted strongly in elevating the sternum, the whole thorax was pulled down and compressed in inspiration, and there was retraction of all the intercostal spaces.

There was no movement of the erector spinæ, and all the abdominal muscles were completely paralysed.

Upper Extremities.—The left upper limb moved normally in every way. The right upper limb was rigidly extended and adducted to the chest wall, the fingers and thumb were flexed, and the forearm pronated. The deltoid, biceps, supinator longus and spinati were much wasted, and no movement could be seen in them. The other muscles of the right upper limb were well developed, and the triceps, pectoralis major, and latissimus dorsi were in a state of tonic spasm. The movements of the fingers were good.

Lower Extremities were much wasted, flaccid, and absolutely motionless.

Electrical Reactions.—There was absolutely no response to faradism in the right deltoid, biceps and supinator longus, or in any of the muscles of the legs or trunk below the level of the second rib, except in the scapulo- and humero-thoracic muscles; and to galvanism all these affected muscles reacted, with A C C > K C C.

Sensation.—There was complete anæsthesia to all forms of sensation below the second rib, and painful impressions were not appreciated in the legs or in the trunk until the level of the second rib was reached, above which it felt. No definite loss of sensation in the upper limbs could be made out.

Sphincters.—The anus was patulous, but urine seemed to be passed reflexly, and did not continually dribble away.

Reflexes.—The knee-jerks were absent. The elbow and wrist jerks were present on the left, but they could not be obtained on the right owing to the position of the limb. The superficial reflexes of the trunk and lower limbs were entirely absent.

The heart and lungs were normal.

On February 23 the child had some bronchitis, and on March 6 it became cyanosed, with great difficulty of respiration, and it died on March 8, after living 15 weeks.

The *post-mortem* was made by Dr. Batten, then Pathologist to the Hospital, to whom I am indebted for the following account:—

Post-mortem Examination.

H. W., aged at the time of death 15 weeks.

The body was thin and the limbs quite flaccid, a slight irregularity of the back could be felt in the dorsal region to the left of the spine. The right arm was rotated inwards, and remained in that position owing to the tense pectoral muscle.

Nothing abnormal could be seen in the cerebrum or membranes. On the under surface of the right lobe of the cerebellum was a small yellowish mass, penetrating into the substance of the cerebellum and having the appearance of an old hæmorrhage. In the 4th ventricle there was some matting and thickening of the membranes, so that the medulla was more adherent than normal to the under surface of the cerebellum. The medulla and spinal cord appeared normal to the level of the 2nd thoracic root. (Plate IV., fig. 1.)

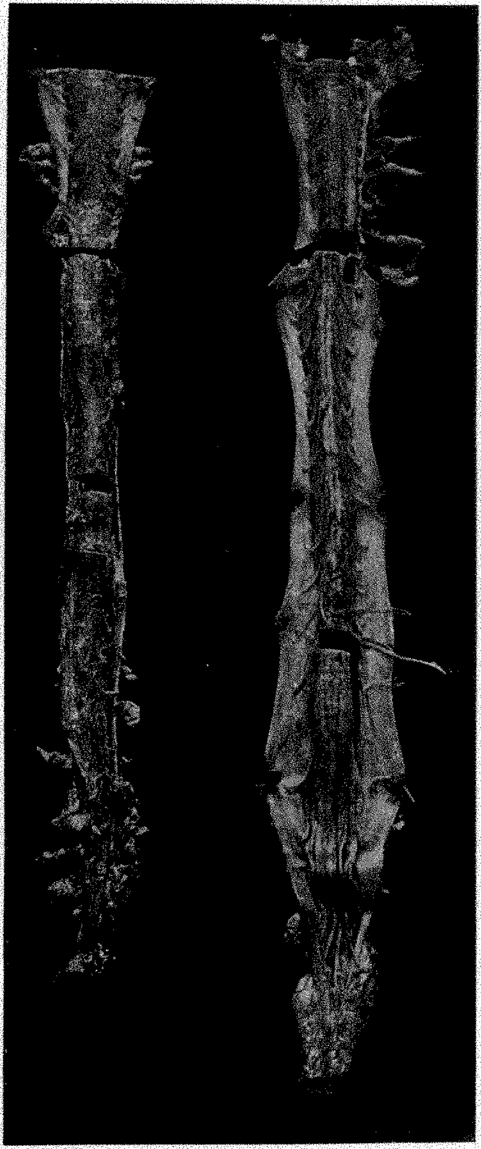
At this level the cord was smaller and felt harder than normal. At the level of the 4th thoracic segment, and extending one or two segments below, the cord felt cystic; below the level of the 5th thoracic to about the 11th the cord felt fairly firm, but below the latter level it was much shrivelled.

The theca was firmly adherent to the cord below the level of the 2nd thoracic, and the lymph was of the same yellow colour as that seen on the cerebellum. The spinal roots could not be separated in the thoracic or lumbar region, and the roots forming the cauda equina were matted together by the same yellowish lymph. (Plate IV., fig. 1.)

Spinal column.—No marked irregularity could be found in the spines of the vertebræ. On examining the bodies of the vertebræ anteriorly, however, it was seen that a dislocation had taken place between the 3rd and 4th bodies, the upper bodies being moved to the right. There was thickening over the 1st, 2nd, and 3rd thoracic vertebræ. There was considerable irregularity in the lateral region of the canal, but it could not be proved that a fracture had taken place, though probably such was the case.

PLATE IV.

FIG. 1. FIG. 2.



Photograph of the spinal cords from the two cases H. W. and W. G.

FIG. 1.—It will be noted that the posterior roots can be seen well in the cervical region, but below the 2nd dorsal they are matted together by lymph over the posterior surface of the cord. The whole cord is smaller than that in fig. 2, although from an older child.

FIG. 2 shows a perfectly normal cord so far as macroscopical appearances are concerned. It serves also as a standard of comparison for the cord in fig. 1.

Fig. 1 represents the cord of a child aged 15 weeks, and fig. 2 that of a child aged 8 weeks (case W. G.)

Both brachial plexuses were dissected out, and appeared to be normal. The right shoulder joint was examined and found to be normal. The biceps muscle of the right arm was, however, much paler and smaller than that of the left.

Nothing abnormal could be found in the thoracic or abdominal organs.

After the cord had been hardened in 10 per cent. formalin, a further examination was made. The total length from the 3rd cervical root to the tip of the cauda equina was 21cmm. The cervical region measured 3·5cmm. to the first thoracic root, and below this point the roots could not be counted.

On section of the cord about the level of the third thoracic segment there was a cavity. (Plate V., fig. 1.) This increased in size and extended downwards for 2cmm., and at it lowest extremity it only occupied the left posterior horn region. (Plate V., fig. 3.) The cavity was filled with gelatinous material which, under the microscope, was seen to contain red blood cells and large granular cells. At a point 11cm. from the 3rd cervical the cord became extremely shrivelled, and this region would seem to correspond to the lower lumbar region.

Microscopical Examination.

Nothing abnormal could be found in the cerebrum, pons, or cerebellum.

At the level of the posterior column nuclei there was marked degeneration in the funiculus gracilis and in the direct cerebellar tract, and this latter degeneration could be traced up into the restiform body.

The degeneration in the funiculus gracilis was so marked that it was best seen by the Weigert-Pal method, while the degeneration in the cerebellar tract was less obvious and showed best by the Marchi method.

A considerable number of degenerate fibres were also present in the funiculus cuneatus, occupying a zone which evidently corresponded to a root, and on tracing this down the cord it was found to correspond to the 5th cervical root. In sections taken through the cervical region the degenera-

PLATE V.

Fig. 1.

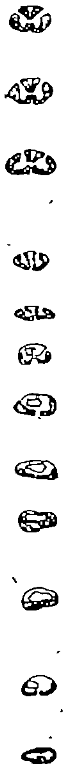


Fig. 2.

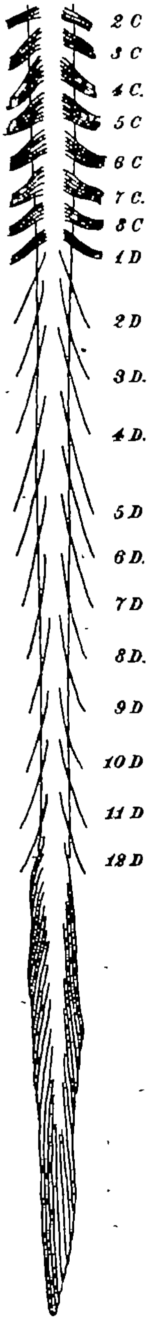
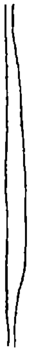


Fig. 3.



Diagrammatic representation of the spinal cord in case 2, H. W.

Fig. 1 represents a series of transverse sections through the spinal cord at various levels in the cervical and dorsal regions, stained by Weigert-Pal method.

The degeneration in the column of Goll is well seen in the cervical and upper dorsal segments. At the level of the 3rd dorsal segment a cavity is seen near the posterior horn which gradually becomes larger, so that at the level of the 6th dorsal segment it occupies the centre of the cord; below this point it becomes smaller, and at the level of the 9th dorsal only remains as a small cavity in the posterior horn.

Fig. 2 is only a diagrammatic representation of the spinal cord in order to indicate position of lesion.

Fig. 3 represents the shape and size of the cavity as reconstructed from the sections at various levels. The cavity extends from the 3rd to the 9th dorsal segment.

tion of Goll's column was well marked (Plate V., fig. 1), the root zone occupied by the 5th cervical posterior root could also be clearly seen, and the degeneration of the direct cerebellar tract was well marked by the Marchi method. Neither of these points are shown in the diagram, which is drawn from a Weigert-Pal specimen. The cells of the anterior horns were well stained, and their chromophilic substance was normal.

At the level of the 2nd thoracic segment the destruction of the posterior columns was complete, and at the level of the 3rd thoracic segment a cavity existed in the posterior region of the cord. (Plate V., fig. 1.)

This gradually increased in size, reaching its maximum between the 5th and 6th thoracic roots, and then gradually became smaller till it disappeared below the level of the 9th thoracic segment. (Plate V., figs. 1 and 3.)

The lower thoracic and lumbar segments of the cord were also completely destroyed, though some medullated fibres existed in this region.

Below the level of the 2nd thoracic segment no normal cells were present in the cord.

Posterior root ganglion.—The cells of the posterior root ganglia stain well by the Nissl method, the nucleus and the nucleolus were normal, and no difference could be made out between the ganglia taken from the lumbar region and those taken from the cervical.

Nerves.—Despite the fact that there was such extensive destruction of the lumbar and dorsal cord, no change could be found in the anterior crural or sciatic nerves of either side by either the Weigert-Pal or Marchi method. Both median nerves appeared normal, but degenerate fibres could be seen in the right brachial plexus both by the Marchi and Weigert-Pal methods. The fibres of the left brachial plexus were normal.

Muscles.—On examination of the left biceps muscle of the arm it was found to be normal; the fibres measured about ·012 mm. in diameter,[1] and were of uniform size, and the transverse striation was well marked.

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[1] The fibres of the biceps muscle from a normal child seven weeks old measured from ·01 mm. to ·015 mm in diameter.

The intramuscular nerves were numerous and well stained, and the muscle spindles were natural, and their nerve supply well shown.

In the right biceps, however, there was a considerable change, some bundles of fibres having undergone marked atrophy, while others remained about the normal size. Some few fibres showed marked fatty degeneration. The muscle fibres within the spindles appeared normal. There was a very marked contrast between the right and left biceps in regard to the number of nerve fibres present, being far fewer in the right than in the left. On longitudinal section the transverse striation of many fibres was well marked, and there was a considerable increase of the connective tissue.

The left biceps femoris, on the other hand, showed most marked atrophy of the muscle fibres, so that in diameter they measure less than ·004 mm.

There was a marked relative increase of the intramuscular nuclei and connective tissue.

The walls of the vessels were greatly thickened and the lumen small. The muscle fibres within the spindles remained normal, and the nerve fibres supplying these were well stained. These were, however, not the only nerves which were stained, for scattered over the transverse section of the muscle other normal nerve-fibres could be seen. One is surprised at the large number of apparently normal nerve-fibres in a muscle so atrophied, although such a condition is not out of keeping with the normal appearance which is presented by the sciatic and anterior crural nerves.

Summary.—The changes found were as follows :—

(1) Dislocation of the bodies between the 3rd and 4th thoracic vertebræ.

(2) Considerable destruction of the cord and matting together of the roots below the 2nd thoracic root.

(3) A cavity in the cord extending from the 3rd thoracic to the 9th thoracic segment, which contained disintegrated blood products.

(4) Almost complete destruction of the cord in lower thoracic and lumbar region.

(5) Ascending degeneration in the columns of Goll and in the direct cerebellar tract, and degeneration in the column of Burdach, corresponding to the 5th cervical root.

(6) Degeneration of some fibres of the .right brachial plexus.

(7) Partial atrophy and fatty degeneration of the right biceps muscle of the arm, and complete atrophy of the left biceps femoris.

(8) Little or no change was present in the larger nerves of the limbs.

The foregoing case is a very good example of severe injury at birth producing dislocation between the third and fourth dorsal vertebræ, with complete destruction of the dorsal part of the cord by internal hæmorrhage, and in addition to this there was stretching of the right brachial plexus, with degeneration of some of its fibres, producing the well-known "obstetrical paralysis" of the deltoid, biceps, and supinator longus, and giving rise to the position of the limb with the adducted shoulder, extended elbow, and pronated forearm, from the overaction of the non-paralysed muscles.

The hæmorrhage into the cord was more extensive than usual, and it is apparently a condition which is the least commonly met with in cases of hæmorrhage affecting the spinal cord. According to Dr. Spencer,[1] who has made extensive investigations on visceral hæmorrhages in stillborn children, out of forty-four cases in which the spinal cord was examined hæmorrhage had occurred in thirty cases, and of these in twenty-one it was found outside the theca, in two between the dura and arachnoid, in six in the arachnoid, in three beneath the pia mater, in four into the anterior cornua, in one into Goll's column, and in only one into the whole thickness of the cord.

I am unable to find a case where the child has lived with such an extensive lesion, or where it has been observed that none of the muscles of the legs or trunk responded to faradism.

With regard to the diagnosis of the two cases, the one last described, and which first came under notice, was considered to be one of obstetrical paralysis. There was the history of a difficult and long labour, with a foot presentation—a condition where there is a liability of traction on the neck—and there was the position of the right arm indicating damage to the brachial plexus; at the same time the flaccid paralysis of the trunk and of the lower limbs and the loss of sensation made it highly probable that there was some injury to the spinal cord. All of these symptoms could be explained by stretching of the right brachial plexus, and a lesion of the cord just below the brachial enlargement.

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[1] SPENCER, HERBERT. "On visceral hæmorrhages in stillborn children."—*Trans. Obstet. Soc*, vol. xxxiii., p. 270.

The diagnosis of the case first described presented more difficulty. Coming under notice as it did, directly after a case which showed symptoms of a traumatic lesion, symptoms which were almost identical in the two cases, it seemed highly probable that this was also due to a lesion of the cord between the 4th and 5th cervical segments, and this view was supported by the history that the birth of the child was attended with difficulty, especially in the delivery of the shoulders, and was partially confirmed by the *post-mortem* examination, which showed that there had been severe damage to the brachial plexus, in fact it was more marked than in the other case.

On the other hand there was the history of the three other children who had been attacked soon after birth by a progressive muscular atrophy, to which they had succumbed in a few months. And although, if in this child the disease was the same, it must have started in utero, and although there was loss of sensation, a condition which was not recorded in the other children, still the strong family history made it highly possible that the pathological changes were of a congenital hereditary progressive kind, and of a totally different nature to the lesions received at birth in the case of the other child here described.

From a clinical point of view it is important to note that almost identical symptoms were presented by a healthy child from severe injuries at birth, and by a child the subject of a progressive atrophy of the anterior horns beginning in utero.

A BRIEF REPORT OF THE CLINICAL, PHYSIOLOGICAL, AND CHEMICAL STUDY OF THREE CASES OF FAMILY PERIODIC PARALYSIS.

BY DRS. JOHN K. MITCHELL, SIMON FLEXNER, AND
D. L. EDSALL, OF PHILADELPHIA.

In 1899 one of us (Mitchell) reported to the Association of American Physicians a study of a case of family periodic paralysis. The present is a brief statement of two other unpublished cases of the same disease, and the results of minute study of the blood, urinary, and gastric conditions in them, and also in the individual furnishing the material for the paper presented in 1899.

Case No. 1.—Mrs. A., born in the United States, aged 35, is an only child. Her father had the same periodic attacks from childhood, but grew better as he grew older. He died of phthisis, aged 40. A paternal uncle was also subject to them. The first attack of the two brothers occurred in childhood and on the same day. No other cases have been known in the family except those hereafter to be described. Mrs. A. had her first seizure at four years of age, but few afterwards until her thirteenth year, since which time they have been of frequent but irregular occurrence. Her general health is poor, and she bears evidence of a healed tubercular process at the right apex. She never has ordinary indigestion, although she suffers from the paralytic seizures if she eats too largely, or of too rich or sweet food, especially the last.

Examination.—A slight, thin woman, somewhat anæmic in appearance; weight 92 pounds. Except for an impaired resonance at the apex of the right lung, with high-pitched inspiration and prolonged expiration, there is no abnormality noticeable in the physical examination.

The knee-jerks are small, capricious, and readily reinforced; arm-jerks and elbow-jerks normal; pupillary reflexes normal;

other reflexes unaltered. Station good; general sensibility wholly unimpaired. The patient's rather anæmic appearance was borne out by the blood count.

When seen in an attack, the symptoms were those of a typical case of periodic paralysis of a not very severe sort. The beginning is usually in the evening; sometimes soon after the evening meal, sometimes later, she begins to have a sense of stiffness, with weakness in the legs, which gradually increases, until she walks or rises from a chair with great difficulty. The anterior thigh muscles are most and earliest affected, so that in an attack, even of slight degree, she cannot go up steps at all. There is no warning of the onset; no pain or soreness; no objective rigidity; often she is unaware of the beginning of a seizure until she attempts a movement. The extent of impairment varies from slight weakness to almost total paralysis. Usually the arms are but little affected, but in the more severe attacks they suffer nearly as much as the legs, but they are never attacked separately from the legs. Sometimes she wakes in the night to find herself completely paralysed. The sphincters are not involved.

The decline, like the onset, is gradual. She seldom has more than one attack in twenty-four hours. If the seizure is severe she is quite certain to be free from any trouble for a day following it.

The attacks can be readily induced by eating sweets, notably chocolates. They are worse if she permits herself to become very constipated. They are increased in severity, if not brought on, by nervous or mental fatigue and worry; but she states distinctly that they are not made worse by exercise, even to the point of fatigue. Indeed, both she and her daughter assert that if they perceive a seizure approaching they can "walk it off." A number of attacks were observed while she was under treatment, differing only in the extent and degree of the paralysis, which was sometimes total below the waist at the height of the attack, sometimes involving the arms in a less degree, sometimes not weakening them at all, and sometimes affecting them equally with the legs. The appearance of the patient is very little changed during an attack, unless it be a very marked one; in that case she looks paler than usual, her circulation is somewhat below its normal force, and her tongue coated. There is no heart murmur, such as is present in No. 3. The power to swallow is unaltered, but she cannot take a full breath or cough voluntarily.

The knee-jerk and the various superficial and deep reflexes peculiar to the areas affected disappear altogether during the attacks. Direct muscle stimulation does not cause contraction. Electrical contractility is abolished in the severe attacks, or, at least, is so slight that nothing short of a violently painful current will produce muscular reaction; when any effect can be had Ca. clc. is always greater than An. clc. In the slighter seizures there is only some impairment of contractility.

Case No. 2.—Miss A. A., daughter of the above patient, aged 13, also an only child, is the fourth instance of the palsy in this family. She is a well-made, ruddy girl, much more strongly built than her mother. At 6 years of age she suffered her first seizure of the family disorder, supposed to be brought on by improper food and over-exertion. She remained free afterwards for about three years, when she had another "fit," and soon after began to have them every three months, always at night, like her mother. In August, 1900, her first menses appeared, after which she had attacks frequently for three weeks. When first seen, October 20, 1900, she was having about two a week. The onset and decline were both gradual as in the mother. She has never been completely paralysed, the enfeeblement being usually limited to the legs, and amounting to great weakness and a sense of stiffening. The arms have rarely been involved at all, and never unless the legs were affected, and the whole attack is much less severe than in No. 1. Sensation is not altered during the attacks. There is no heart murmur. The mental functions are in no way disturbed in either patient. The mother is worse just previous to her menstruation; the girl has her worst attacks during that period.

The electrical statement made for the mother will answer for the daughter, namely, that there is an impairment of all forms of contractility.

The girl is not anæmic.

The urine in both patients during an attack is scanty, loaded with urates and uric acid, and of extremely high acidity, but otherwise normal to ordinary examination. On one occasion a faint trace of albumen was found in the girl's urine during an interval.

Case No. 3.—C. H. J., now 21 years of age, was fully reported two years ago. His first attack occurred in his thirteenth year, and he is the fifth person in three generations of his family known to have suffered with these seizures, viz., his mother, his maternal grandfather, a maternal uncle, and a maternal first cousin (a girl, aged 15). They have happened since their original onset in steadily increasing numbers. When he was seen in October, 1898, they had returned with remarkable regularity about once a week for some weeks. They were somewhat irregular while under treatment in the Infirmary for Nervous Diseases, but since he left the hospital in the spring of 1899 they have re-established about the same periodicity.

If there is any difference between the attacks at the present moment and those occurring three years ago, they are now somewhat more severe and more prolonged than they were then. They still usually begin at night, perhaps with some precedent warning in the shape of slight weakness of the legs in the afternoon or evening. The only difference in the symptoms is that the heart murmur, at that time heard only in the attacks, is now constant. This is a systolic murmur limited to the pulmonary area and transmitted somewhat up and down the left side of the sternum, and a split second sound heard best at the second interspace, lessening in intensity towards the apex. No alteration in the outline of the heart is demonstrable by percussion.

His general appearance during an attack is peculiar. He becomes pale, even his lips losing colour, his tongue is coated, his breath heavy smelling and unpleasant; he has no desire to take food, and experiences some difficulty in swallowing during the attack. There is a question of whether the involuntary muscles as well as the voluntary are affected, as he cannot take a long breath, or cough or sneeze, and has trouble in voiding urine, though these difficulties may be wholly due to the palsy of voluntary muscles. Patellar, abdominal, testicular and elbow reflexes are abolished; the electrical reactions entirely lost to every form of stimulation short of a dangerous and painful current while the paralysis lasts. When he begins to improve, the attack passes off very rapidly, so that in half an hour or less he becomes entirely able to get about, his reflexes and muscular reactions are regained, and he feels perfectly well except for slight muscular soreness.

It has been noted this time that the impairment, if not the loss, of the knee-jerk seems to persist for hours after he has begun to improve in other respects, and it sometimes has been difficult to elicit even when he was able to be up and walk about the ward. The young man himself describes the attacks as at present more complete and lasting somewhat longer than has previously been the case, the duration, formerly twenty-four to thirty-six hours, being now usually forty-eight, and occasionally even longer.

Patient No. 1, an intelligent, well-educated woman, had made for herself the interesting observation that citrate of potash in good-sized doses would cut short an attack. This, together with the extremely acid urine of patients Nos. 1 and 2, suggested a study of the alkalinity of the blood and urine, and at first we thought we had secured interesting results, which have, however, not been confirmed by subsequent study. We will describe these results in more detail later.

We examined also the effects upon rabbits of injection of blood serum from patient No. 1. Our intention was to inject serum taken during a paralytic period and endeavour to discover if any effects were produced by it upon the knee-jerk in rabbits.

Forty cc. of blood were drawn from the median basilic vein of Mrs. A. by a sterile syringe and placed on ice in sterile vials. Forty-eight hours later it was centrifugalised to separate the serum completely.

After some work to determine a sort of normal curve of knee-jerk, 4 cc. of the serum was given into an ear vein of a rabbit and a series of tracings made of the knee-jerk as elicited at intervals for forty-eight minutes after. No effect upon the knee-jerk could be observed.

A second injection of 3 cc. was given to the same rabbit a little over an hour after the first. Tracings made five, twenty, and twenty-eight minutes after showed no decided change from the normal record. When forty minutes had elapsed the knee-jerk seemed *more* irritable than normal. Much muscle tremor was noticeable and somewhat interfered with the clearness of the tracings.

It was curious to note that crossed reflex was very constant in both the rabbits used. The injected rabbit was found dead the next morning. The lethal dose of human serum for the rabbit may be below ·1 per cent. of body weight. A dose of normal serum of the same size would probably have destroyed him in the same time.

A second series of experiments was made ten days later, with blood drawn during another and much more severe attack. The patient's blood on both occasions flowed very badly, and it was necessary to introduce the needle a second time into another vein to secure the desired amount.

Injections were made into rabbits in (1) the femoral artery, the vein being ligatured. No difference could be noted between tracings made before and after the injection, or between the injected and the untouched side. (2) Into the anterior thigh muscles. No effect. (3) After trephining, an injection was made under the cerebral meninges. No effect upon the knee-jerk could be discovered an hour later. (4) Serum injected into the spinal canal in lumbar region at two different levels. No effect. (5) Injection into the sheath of the left sciatic nerve. A trifling increase of knee-jerk was observed twenty minutes later, probably due to irritation from the operation of exposing the nerve sheath.

These experiments (given only in outline) were wholly inconclusive, and not in any way satisfactory. We think it possible that rabbits were not the best subjects, and that animals with digestive tracts and food habits more nearly approaching the human type would be more suitable and perhaps give results of more value.

It is, however, interesting that the few trials undertaken confirm the negative results of the attempts of one of us (Mitchell) to find toxic qualities in the blood or urine of case 3 when previously studied in 1898-99.

Blood examinations were made in patient No. 1 to determine the alkalinity of the blood. Only two determinations could be made, one during the attack, one during the interval. In both of these Löwy's method was used. The woman showed in the interval an alkalinity equivalent to

464 mg. of soda; during the attack the alkalinity was 224 mg. The former figure is distinctly high, but the latter not unusually low, or, at least, not low enough to be considered indicative of acid intoxication. She had been using alkalies internally in full doses until forty-eight hours before the first estimation; possibly the high alkalinity was due to this, and the second figure represents more nearly the patient's normal.

In the second case no examination of the blood was made. In the third the examination in three attacks practically showed no difference in the alkalinity, the figures being respectively 512 in an attack, in the interval 496, and in the next attack 504—all somewhat high figures.

The urine in patients Nos. 1 and 2 during an attack showed a condition of such marked acidity as to suggest the need of more minute study of the acid secretion. Accordingly it was carefully investigated for acetone, diacetic acid, and lactic acid. The results were negative in all these examinations.

More important negative results still were obtained from the estimation of the ammonia of the urine in No. 3. The figures for twenty-four hours never passed 1½ grammes of NH_3, except in one instance when over three grammes were passed, and this latter was a doubtful examination owing to some carelessness in the preservation on that day. The ammonia (NH_3) was estimated through five attacks and their corresponding intervals. Preceding the first attack in which this was done, the figures for several days were astonishingly low considering his diet. The urine contained only about 100 mg. of ammonia, or even less—a very low figure. Since muscle metabolism would seem to be an important source of the acids produced in the body and is perhaps one of the chief sources, the low ammonia figures suggested that there might be decided qualitative or quantitative alterations in muscle metabolism before as well as during the attack.

Tests of the toxicity of the urinary secretion were made during the height of an attack, and the blood serum taken during the same attack was tried at the same time. In neither substance could any increase of toxicity be demonstrated, rabbits surviving the injection without any apparent effects.

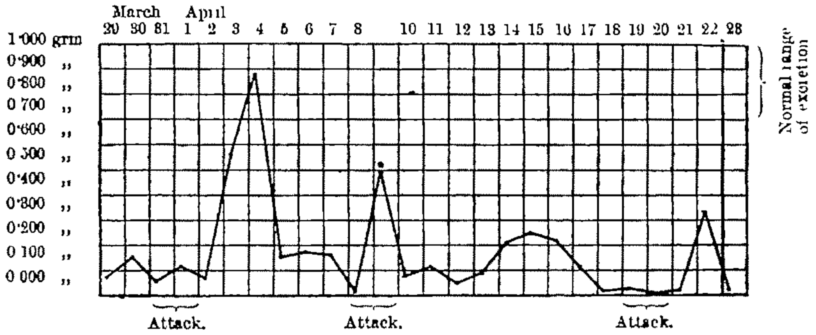
The examination of the stomach contents of No. 1 on two occasions gave one curious result, viz., even starch digestion was not proceeding and there was a total anacidity, showing the whole digestive process to be absolutely at a standstill, and the gastric motor power diminished or abolished for a time.

The low ammonia content of the urine suggested to Dr. Edsall to make daily estimations of the keratinin excretion, hoping thus to discover something of the causation of the disorder. The Neubauer-Salkowski method was used in all the determinations.

Our knowledge of variations in the excretion of this substance is not great. Normally on mixed diet the excretion usually runs from 700 mg. to 1 gm or above. In muscular dystrophies, extensive paralysis, and other conditions in which the activity of the muscles or their bulk is largely reduced, the excretion is much below the normal, while during the process of wasting of muscles, as in cachexias, and also after severe over-exercise, the amount increases. Diet also influences the excretion largely, and further, very severe anæmias are accompanied by an extremely low excretion. With the exception of the condition in anæmias, practically all these points, as well as the fact that kreatin, from which kreatinin is derived, is found in large amounts in muscular tissues only, indicate very strongly that these substances are in chief part, at any rate, products of muscles, and possibly are produced practically solely by the muscles. The conditions in severe anæmias do not, of course, necessarily contradict this view, as metabolism in general is so largely disturbed in such disorders. While, then, the excreted amount in the normal human urine is undoubtedly derived largely from the food, there is good reason for believing that a large part of the normal amount is derived from the body muscles, and that this amount varies largely with variations in the condition of the muscles.

The results of the estimations are shown roughly in the chart. There is in each instance a period of several days of extremely low kreatinin excretion preceding the attack and lasting into the attack and beyond it. Following this there is a sudden rise of the excretion from a point ranging between 3 and 80 mg. up to as high as 880 mg., and then, after reaching this normal or nearly normal level, the excretion falls again and a similar course occurs once more. The abnormal figures are evidently not due to the attack, as they precede it, while those figures approaching the normal occur directly after or with the attack. The very striking relation of the kreatinin excretion to the attacks is evident throughout the series of estimations, and it seems almost unquestionable that in this case, at any rate, the kreatinin is an index at least of alterations in metabolism which lead up to a seizure, and are followed by conditions approaching the normal. The cycle then begins again. The relation of the kreatinin to attacks and intervals is most evidently seen in the unusually long period intervening between the second and third attacks. The kreatinin figures rise at the end of the second attack and then fall at once, but there is another rise which, though relatively slight, persists for

Chart of Kreatinin Excretion—Periodic Paralysis.



* This figure is certainly too low. Some of the urine (about one-fourth) was sent to Dr. Flexner. The actual figure when reckoned for the whole amount of urine would be 668 mg.

three days, and apparently is the evidence of sufficient improvement in his condition to postpone the onset of the next attack, for this interval was three days longer than the usual one. This correspondence between the rise of the kreatinin excretion and the period of freedom from paralysis is curiously striking. A somewhat similar relation may be observed between the relatively low rise in excretion at the period of the third attack and the brevity of the freedom from symptoms following this low excretion. While there was not an actual attack the man had all the usual feelings of an approaching attack on the fifth day after the seizure (on April 24), and was unwilling to go out of the hospital because he feared he would be overtaken by his paralysis. As just noted, the rise in kreatinin excretion with the end of the preceding attack had been relatively slight and had not persisted.

The changes in kreatinin excretion might possibly have been explained on the basis of alterations in the amount or character of the food taken or have been considered the result of the temporary absolute disuse of the muscles had these changes occurred only immediately within the period of the attack, but the striking fact about the kreatinin figures is that they were extremely low for a number of *days before each attack* when the man was taking full diet, and the rise in excretion in the second attack shown on the chart came actually within the period of the attack itself, and consequently within the time of practically total abstinence from food and total disuse of the muscles.

Further, the relation of intake of nitrogenous foods to the kreatinin excretion was controlled by coincident daily estimations of the total nitrogen of the food (Kjeldahl method) the results with the nitrogen demonstrating that the total decomposition of nitrogenous food and tissue was at least as high during the periods of low kreatinin excretion before the attack as it was at other times, the only actual falls in excretion of nitrogen coming during the period of the attack, when he was taking very small amounts of food. Another possible source of error that has to be considered was that some of the kreatinin might not have crystallised out as kreatinin zinc-chloride on the days of apparently low excretion, and had been lost in the filtrate. But that this was not the case was shown by using Weyl's and Jaffe's tests with the alcoholic filtrate. Only faint traces were ever found during these periods, and one finds traces dissolved in the filtrate under ordinary circumstances.

So far then as general conclusions may be reached from the study of one case, it may justly be considered that the attacks are due to metabolic disturbance and that this disturbance may be situated chiefly, or primarily, perhaps entirely, in the muscles themselves. Our knowledge of the excretion of kreatinin in disease is not sufficient to indicate whether the disturbance ultimately producing an attack does or does not begin in the muscles alone; it seems distinctly probable, however, that there is a disturbance in the metabolism of the muscles preceding the attack, whether there is more general metabolic disturbance or not, and, at any rate, it seems practically clear that the present disorder is one of metabolism. A rather striking analogy with gout may, of course, be readily drawn at once, though the variations in the kreatinin excretion in this case are more striking than any that have been well demonstrated in the uric acid in gout. Whatever be the cause of the variations in the excretion of uric acid in gout, it cannot be reasonably suspected that the disturbance in this case is due solely to *retention* of kreatinin or kreatin. The figures seem to demonstrate that it is not possible that such is the case; they must be due either to a reduction in the formation of these substances or to their abnormal destruction within the body. The figures are so extremely small that the latter seems the more probable explanation, for some of the kreatin of the food, which is normally excreted as kreatinin, must, in this case, have been excreted in some other form, probably as urea. There is no reason for believing that a retention of kreatin would produce these symptoms, for it is non-toxic, and there is no good reason for thinking that kreatinin could cause any notable tonic effects. There is a possibility from Ranke's work that kreatinin itself has some influence on muscular contractility in this case, and this possibility will be the subject of further study. It is wholly probable, however, that the alternating in kreatinin excretion in the case can only be considered to indicate the existence of disturbance of metabolism and that kreatinin itself has no influence in producing the attacks. Some further study of these questions is, of course, intended, but it has not been possible to complete it before presentation of the present paper and this brief outline of our findings.

It would be interesting to know the effect upon the attacks of moderately severe *over*-exercise a day or two *before* the expected attack. It is possible that this might serve to stimulate metabolism sufficiently to postpone the attack at least, though it might produce just the opposite effect. Some support is given to this theory by the statements of patients, not only ours, but E. W. Taylor's and some of the German cases; that exertion would temporarily postpone an attack, often at the cost of a seizure of greater than the usual severity after. This is not incompatible either with the other observation, that exertion in certain instances has *induced* the paralysis.

It is also very important that we should learn the condition of kreatinin excretion in epilepsy, myasthenia gravis, and some other conditions which promise to teach us some new facts concerning its relation to disease.

The practical aspects of the cases as to treatment are interesting and highly unsatisfactory. In No. 3 strict diet, baths, and exercise made no change in the periodicity or length of the attacks. Colon lavage and intestinal antiseptics by the mouth were no more successful. Quinine, bromides and strychnia were administered at different times, and the results again were negative. The slow flow and the dark colour of the blood when venesection was performed suggested hypodermoclysis, which was twice tried without good effect. As already noted, patient No. 1 had observed that citrate of potash had a favorable influence. As a prophylactic, citrate of potash seemed to have some small but uncertain effect in Nos. 1 and 2 in doses of 45 to 60 grains a day. In No. 3 it did not reduce the frequency of occurrence.

Administered at the beginning of a seizure in repeated large doses, it certainly shortened and mitigated the paralytic period in all three patients. The attacks were so much more regular both in recurrence and duration in No. 3 that it was easier to judge. His seizure occurred every seventh or eighth day with great punctuality, and lasted almost exactly forty-eight hours, the shortest one which was observed without interference being about twenty hours; but this was the only one out of twelve which extended to less than thirty hours. It is therefore fair to infer when four attacks treated with the potash salt only endured twenty-four hours each that this shortening was due to the drug. Another attack during this period treated by hypodermoclysis ran, as usual, close to forty-eight hours. It is curious that with No. 1, and to a less extent with No. 2, a similar though not so marked influence upon the seizures was shown by bromide of potash, a drug which did not prove of any value in case No. 3.

In view of the fact that citrate of potash is absorbed as the carbonate, it was thought that a quicker and perhaps stronger effect would be produced by the latter salt. This did not prove true when tried in practice, the attacks being much less influenced by the carbonate than by the citrate. Through a druggist's error on one occasion, patient No. 1 took chlorate of potash in place of citrate. The result was not quite so favourable as when the latter salt was used, but better than when the carbonate was given. Bicarbonate of soda was tried on several occasions, but seemed to have little effect.

In conclusion, we would reaffirm the statement already made, that our endeavour has been to state facts as we have observed them, and not to propound a theory. The time for theorising must be postponed until further study is possible of this curious condition and some of its possible analogues.

OBSERVATIONS OF A CASE OF CONVULSIONS. (TRUNK FIT OR LOWEST LEVEL FIT?)

BY J. HUGHLINGS JACKSON, M.D., F.R.S.,

AND

H. DOUGLAS SINGER, M.D, M.R.C.P.

THE following case is of interest from two points of view: (1) the association of "epileptic fits" with congenital syphilis, and (2) the kind of convulsion. That the convulsions occurred in a patient the subject of inherited syphilis is, of course, of great importance. It does not, however, necessarily follow that the patient's attacks were owing, directly or indirectly, to syphilitic changes in some part of her nervous system. In this paper we remark almost solely on the patient's fits.

The state of the respiratory apparatus in "epileptic" paroxysms has received little special attention, even in cases of so-called cortical (Bravais) epilepsy fixation of the chest may be overlooked. In a case of this kind of epilepsy observed by one of us there was—along with the convulsion starting in one hand and affecting the whole of the arm, with turning of the head and eyes to the same side—complete fixation of both sides of the chest; this occurred in paroxysms of the range mentioned, during which the patient was not unconscious.

One of us (J. H. J.) has suggested that, besides what are commonly called epileptic fits, there occur, in the human subject, bulbo-pontal (lowest level) fits, analogous to those experimentally produced in some lower mammals. With regard to proving or disproving this hypothesis, it is, among other things, particularly important to note where the first spasm is, or what the very first symptoms are. Are there seizures, such as would be commonly called epileptic, which *begin by* fixation of the chest, or in which the chest is involved before the limbs, if these are involved in the seizures; or, speaking more generally, are there fits which begin by convulsion of respiratory muscles?

The case we are about to report is an example of fits of this sort; it is clear that, in many of this patient's attacks, the first symptoms were involvement of muscles of both sides of the neck (back and front), soon followed by fixation of both sides of the chest. The neck muscles may have been engaged by discharge of central nervous arrangements representing them as they serve respiratorily—that is to say, as they serve in difficult respiration. And, what is particularly significant, in many of this patient's attacks, those during what we shall call the First Period, the limbs were not affected at all, although the trunk muscles of both sides were strongly engaged. Were this patient's attacks bulbo-pontal fits? There is another possibility: the seizures may have been owing to a discharge lesion of some part of Horsley and Schafer's trunk centres. There is yet another possibility. Recently Sherrington and Grunbaum have discovered, in the chimpanzee, a trunk centre in the external surface of the Rolandic cortex, between the arm area and the leg area. They write (*Brit. Med. Journal*, December 28, 1901), that they "find between the representation of shoulder and hip an area which, next to the shoulder, yields unilateral movement of the chest muscles, and, next to the hip, yields unilateral movement of the abdominal muscles." If there be a trunk centre in the Rolandic region of the human brain, the discharge lesion in our patient may have been of some elements of it. It is true that the movements Sherrington and Grünbaum produced were unilateral, but possibly an intense ("an epileptic") discharge beginning in their Rolandic trunk centre of but one half of the brain might produce bilateral convulsion of the parts they mention.

There are difficulties in the way of each of the hypotheses we have stated; we prefer, whilst giving in great detail particulars of the attacks our patient had, to refrain from speculations on the localisation of the lesion causing them. We may, however, say what the question is.

It is of little moment whether the fits are to be labelled "epileptic" or not. Admitting that the slight fits (*vide infra* 4) in which there was movement of the eyes and no fixation of the chest, offer a difficulty, the question as to the severe fits is, "Where is the lesion (discharge-lesion) which, on its occasional "intense" discharge, produces a convulsion *beginning* in muscles of the trunk (that is, in muscles of two sides of the body, the normal action of which may be and often is bilateral) and beginning in those muscles of the two sides of the body simultaneously—a convulsion in some paroxysms (first period) not involving the limbs at all, and in others (second period) involving both arms *after* the trunk, involving these limbs simultaneously; also, what is very significant, involving the muscles of the arms from above downwards, thoracico-humeral muscles to those of the hand.

We have considered it advisable to describe the fits under two headings, for two periods, because as the seizures diminished in number they became modified in character. We wish particularly to lay stress upon this division, because, although there were some slighter fits of somewhat different nature common to both periods, no attacks such as those which formed the main feature of the Second Period occurred as far as our observations went, and they were numerous in the First Period. The following order will be followed:—(1) The history of the case; (2) the results of the general examination of the patient; (3) a description of the fits occurring in the First Period; (4) a description of the slighter attacks occurring in both periods; (5) an account of the seizures in the Second Period.

(1) History.

J. K., aged 17, is the eldest of a family of nine. Her father, mother, brothers and sisters are all living and healthy; the mother had no miscarriages until the last nine months, during which time she has had two. Most of the children are said to have a "narrow bridge" to the nose and several of them had snuffles in infancy, but none of them, as far as the mother can remember, had any rash. None have had any troubles with their eyes.

The patient was born at full term and without instrumental help; she had snuffles, but no rash as an infant; she has always had a squint which is said to have been worse since the onset of the fits. She was backward in walking, not beginning to do so until 3 years old, but she began to talk at the same age as her brothers and sisters, viz., 12 months. She has suffered from whooping cough, measles and scarlet fever. During the first dentition for about two years she had "teething convulsions" at intervals, in which she is said to have been quite quiet and "looking dead"; there were never any twitchings in these attacks.

The present illness began at the age of 9 years; the fits at first occurred about once a month, gradually increasing in frequency at the onset of puberty at the age of 15 years to about one a week. After this they rapidly increased in number up to several daily. In March, 1901, she was in a condition of *status epilepticus* for ten days, followed by a period of complete freedom from fits for a month, after this time the fits again increased in number until four days before she came under our observation on December 20, 1901, when she once more passed into *status epilepticus.*

(2) General Examination.

When first seen she was having a fit about every ten minutes, with recovery of consciousness but not of much mental power in the intervals. The general examination was not completed until December 22, the time being devoted to the observation of her fits. At this time she had had no fit for half an hour and would obey simple orders and answer simple questions. She was, however, extremely fatuous, with very bad memory, and had difficulty in fixing her attention.

She is dark, with muddy, coarse skin; the forehead is large, square and overhanging, the bridge of the nose flattened and the nostrils thick and snub. The lips are coarse, thick and habitually parted, the upper teeth projecting over the lower lip. The lower part of the face is thin with pointed chin and forms a striking contrast to the large forehead. She breathes habitually through the mouth, but can blow down her nose The tonsils are not enlarged and neither they nor the fauces show any scars of past ulceration. The palate presents a high, narrow arch. The left upper median incisor tooth shows a well marked notch and narrows gradually from base to cutting edge (the kind of teeth described long ago by Hutchinson). The pupils are large, equal, and re-act to light and in convergence; they dilate well under homatropine and show no iritic adhesions. There is a well marked convergent strabismus due to weakness of the right external rectus muscle; Mr. Marcus Gunn agreed with us in this observation and inference. The fundi were examined under a mydriatic by Mr. Gunn after the fits had ceased. He reported as follows:—"The corneæ are hazy and there are remains of vessels running into both—undoubted evidence of old interstitial keratitis. The fundi show numerous patches of choroidal atrophy of typical syphilitic nature, and the optic discs show the usual atrophy secondary to that condition of the choroid."

The patient's *power* generally is feeble, but except for the weakness of the right-external rectus muscle there is no paralysis and certainly no unilateral weakness, all *movements* are present and well co-ordinated. *Respiration* is of the type normal in her sex—that is to say her inspiration is mainly upper thoracic; there is some widening of the costal angle and slight protrusion of the abdominal wall. In the act of drawing a deep breath, that is when told to do so, the movement is mainly upper thoracic at first, the sterno-mastoids being used; but towards the end of this voluntary act the diaphragm descends and the abdominal walls are pushed forward. *Sensation* appears to be normal in every way. The knee-jerks, when the patient was first seen, were well marked but not exaggerated, equal on the two sides, but when examined two days later and at some considerable time after a fit, they were obtained only with difficulty; this was also the case after complete cessation of the fits for three weeks. There was no ankle or rectus clonus. The *plantar reflexes*, both feet, were definitely extensor in type, but after complete cessation of the *status epilepticus* they were flexor in character. The *feet* show a high arch with some extension at the metatarso-phalangeal joints and flexion of the distal joints. This was said by the mother, in answer to questions, to have always been the same.

The *lungs* showed no sign of disease; it was particularly observed that there was no emphysema and no deformity of the chest. The heart sounds were everywhere clear and without murmurs, but tended to approximate to the fœtal type, that is to say, the character of the two sounds were very similar and the intervals were nearly equal. The *pulse* was regular, soft and easily compressible, its rate being about 100. Nothing abnormal was found on examination of the abdomen.

(3) Fits occurring in the First Period.

The duration of each fit was very brief, and their frequency being very great particular attention was paid to different points in different seizures. We shall first give accounts of some of the individual attacks copied almost verbatim from the notes made immediately after each observation, and shall then describe an attack compounded from the notes taken of numerous fits.

Descriptions of Individual Fits.

(1) At the moment when first noticed there was tonic spasm of the muscles of the neck on both sides, back and front, of the jaws and of both sides of the face, while the thorax was fixed in a position of partial expiration. The jaws were separated so that there was an interval of about half an inch between the teeth while both masseters and both mylo-hyoid muscles could be felt to be firmly contracted, contending against one another. The eyebrows were raised and the eyes, still maintaining the convergent strabismus noted above, were directed upwards. After a few seconds the tonic was replaced by clonic spasm affecting the whole face (the angle of the mouth being drawn a little more to the left than to the right), also the muscles of mastication, the sterno-mastoids, and the muscles at the back of the neck on both sides. Here is to be mentioned a point of great importance. *No movement or spasm of any kind occurred in the arms; they remained quite flaccid and loose.* The legs were not specially observed in this fit, but there was no obvious movement. As the fit passed off several deep inspirations were taken. Immediately afterwards the patient was asked to draw in her breath voluntarily, but appeared not to understand, and merely replied, "Yes, thank you."

(2) This fit began while I (H. D. S.) was auscultating the chest, and consequently it was observed from the beginning. The stethoscope was retained over the heart and attention was also directed more particularly to the face and neck. The patient was lying at the time on her back with her head turned to the left. The first motion consisted in a slow rotation of the head to the middle position with a little drawing down of the occiput by the muscles at the back of the neck, whilst at the same time both sterno-mastoids were seen to stand out prominently. Almost at the same moment, but I think a little later, the face muscles were contracted in tonic spasm, the eyebrows raised, the angles of the

mouth were retracted a little, somewhat more to the left than to the right. The eyes, with the convergent strabismus still present, were rotated upwards, the right being mesial while the left was rotated inwards. The teeth were separated by about three-quarters of an inch, the jaws were rigidly fixed and the mylo-hyoid muscles were felt to be firmly contracted. The tongue could be seen and did not appear to be contracted in tonic spasm, and certainly was not involved in clonic spasm later.

Respiration had ceased from the time the earliest motion was observed; and as the head moved round towards the midde line, a moaning noise was produced by, as proved by holding the hand in front of the nose and mouth, air being forced out of the chest.

After a few seconds clonic spasms replaced the tonic contraction in all the affected muscles, viz., face, jaw, neck and mylo-hyoids; at this time air was sucked into the chest with a grunting noise, as if through an almost closed glottis, by each clonic jerk. The spasm in the thoracic muscles then ceased and several deep breaths in succession were taken. The clonic spasms of the face and jaw muscles continued for a few seconds after the onset of the deep breathing and ceased last in the orbiculares palpebrarum and the frontales muscles.

The heart sounds were listened to occasionally through the binaural stethoscope; at the height of the tonic stage, just before the clonic spasms began, the heart was beating at a rate which I (H. D. S.) estimated at 60 per minute. When counted shortly before the fit the pulse rate was 102 per minute. When the clonic spasms began the noise of the contracting muscles and of the indrawing of the breath prevented the heart sounds from being heard, but immediately after the fit the rate was 120 per minute. The arms and legs were not watched in this attack.

(3) The patient was lying on her right side apparently asleep. As I (H. D. S.) approached the bed there was a slow conjugate movement of the head and eyes to the left. The limbs being covered nothing could be seen of any movement or spasm, but through the clothes there did not appear to be any movement of them. The corneal reflexes were present when I (H. D. S.) reached her and the head slowly came back to the original position and the patient began to mutter inarticulate sounds. A few seconds later one of the attacks similar to those described above began. Attention was at once directed to the pulse and to the erector spinæ muscles, which could easily be observed as she was lying on her right side. At the moment of feeling the *pulse* the tension seemed higher than when examined at other times

and it distinctly increased, while the pulse rate became slower until the clonic stage was reached, when the tension markedly dropped and the rate became much more rapid.

Although the muscles at the back of the neck could be felt to be in a state of tonic contraction and later in the seizure were seen to undergo clonic spasm, I (H. D. S.) was unable to satisfy myself that there was any spasm in the muscles lower down the spinal column.

In other fits attention was directed specially to the condition of the limbs, the abdominal muscles, the degree of expansion of the thorax, the colour of the lips, and the presence or absence of sweating about the forehead.

Description of the character and course of the Fits compounded from all the observations made at different times during the First Period.

For convenience the fit may be divided into three stages: the tonic, the clonic, and the stage of recovery, although the three merge into one another and in part overlap.

Stage 1.—Tonic spasm occurred first in the muscles of the neck, followed almost at once by spasm of the muscles of respiration, causing complete fixation of the thorax. Then followed spasm of the face, the jaw, the mylo-hyoid and the abdominal muscles; and for all these it was impossible to determine any definite order. It is to be understood that the spasm of all the regions involved was of both sides at once and, except for the muscles of the face, of both sides equally. These several muscular regions will now be considered seriatim.

Neck.—The head was rigidly fixed in the mesial position, with the occiput drawn a little downwards and backwards as a result of the contraction in the muscles in the back of the neck, while both sterno-mastoids stood out prominently.

Respiratory Muscles.—As the spasm involved these muscles there was a brief moaning expiration, evidently through an almost closed glottis, ending with complete fixation of the thorax, and thereby arrest of all respiratory movement. The degree of expansion of the chest when this arrest occurred was in most observations below the mean between full inspiration and full expiration, but on two or three occasions it was noted that the thorax was expanded rather more than the mean.

Abdominal Muscles.—These were found to contract and to become firmer and more resistant, but the degree was never great.

Face.—The eyebrows were raised and the angles of the mouth drawn outwards; generally, if not always, more towards the left than the right side.

Jaws.—The masseters were felt to be strongly contracted, but the teeth were separated by about half an inch, indicating powerful spasm in the depressors of the lower jaw. No deviation of the mandible was noted, although on one occasion there was some doubt as to whether it was not directed a little to the left. The mylo-hyoid muscles were rigidly contracted.

Eyes.—The internal strabismus due to weakness of the right external rectus muscle was always maintained, and the eyes were strongly rotated upwards, the upper lids being also elevated.

STAGE 2.—Typical clonic spasms followed the tonic contraction in all the affected muscles, including in some attacks, but not in all, the respiratory muscles; when they were so affected air was sucked into the chest by each spasm, causing a grunting noise. The abdominal muscles were never observed to undergo clonic spasm.

STAGE 3.—*Recovery.*—As the fit passed off, the spasmodic fixation of the thorax ceased first and there then ensued one or more deep breaths; it was considered probable that the depth of inspiration was greater at this time than when the patient was asked to draw a deep breath during an interval between two attacks. On several occasions she was told to draw a deep breath immediately after a fit was over, with a view to determining whether or not there was any weakness of the respiratory muscles as a sequence of the previous spasm—such weakness as is seen in a limb after a seizure due to (remaining after) some local cortical discharge. But on no occasion could she be induced to draw in her breath when told; the shortest interval between a fit and the performance of this voluntary act was about five minutes. The non-compliance with this request was probably due to the mental state, as she made no attempt to make the movement and generally answered "Yes," or "Yes, thank you." With regard to the order in which cessation of spasm occurred in the other muscles, the only observation on this point is recorded above when the last muscles to relax completely were the frontales and orbiculares palpebrarum.

The *pulse* was observed to become slower in rate but of higher tension up to the time when the tonic spasm of the thoracic muscles gave away; there was then a notable and rapid fall in the tension and a marked increase in the frequency leading to a more rapid rate than had been present before the seizure.

Reflexes.—The corneal reflex was definitely lost and probably unconsciousness was complete. The knee jerks became a little more marked during a fit, but were never much exaggerated. The plantar stimulation yielded extensor responses which continued to obtain between the attacks until the *status epilepticus* ceased.

So far we have dealt entirely with the positive results of the observations, but there still remain the equally important negative results. The *limbs* were very carefully examined, the sister examining the thighs both with hand and eye in many attacks, and we are confident that *there was no spasm of muscles and no movement of the limbs of any kind whatever at any time during the attacks;* both arms and both legs remained absolutely flaccid throughout the seizures. *No definite change of colour* in the face or lips could be determined, although frequently looked for, and there was *never any sweating* of the head or face either to be seen or felt.

The duration of the fits varied a little, but may be stated roughly to have been forty to sixty seconds. When the fit was over the patient remained in a heavy, stupid condition for some minutes and often until the onset of the next attack. She would, however, sometimes obey simple commands, but never spoke rationally, her almost invariable reply to any remark being "Yes" or "Yes, thank you."

(4) Slighter Fits occurring in both periods.

On the fourth day after we first saw the patient some very short fits were observed for the first time; they continued to occur with considerable frequency from that time onwards. One of these is briefly described above as occurring just before the onset of fit 3 in our account of the individual fits of the First Period. These slighter seizures were very brief, lasting only a few seconds and consisted in a slow conjugate deviation of the head and eyes; this movement was generally towards the left side, but on several occasions it was towards the right and then the convergent strabismus was still maintained, the right eye moving only a little beyond the median position, whilst the left well into the inner canthus. A very fine symmetrical rotatory nystagmus was seen in the eyes in some of these slight attacks; and flushing of the conjunctival vessels with some lachrymation was also noted. There was no fixation of the thorax in these attacks, although on one or two occasions it was thought that respiration became a little slower, but of this we are not certain. No spasm was observed in any other muscles.

(5) Fits of the Second Period.

The first of this series of attacks was seen on the sixth day after the patient came under our observation, and even at the risk of being accused of too much repetition we must reiterate that no attack such as that described below, that is with convulsion extending to the limbs, was observed during the First Period. The seizures in the Second Period differed from one another only in severity, hence it will be unnecessary to do more than give one description compounded from all our observations, which were not nearly as numerous as in the case of the fits in the First Period because the frequency became progressively less.

The first change observed in these attacks was a sudden and complete fixation of the thorax with arrest of all respiratory movement; this was followed by spasm, on both sides of the body, of the muscles of the face, jaw, neck and upper extremities, and in some cases, but not in all, also of the muscles of the lower extremities. The spasm, at first tonic, very shortly became clonic. The head was retracted and there was sometimes conjugate turning of the head and eyes to the left, although both sterno-mastoids contracted. The upper extremities were not affected until the tonic contraction in the muscles of the face, jaw and neck had given place to clonic spasm; *the order in which the muscles of the arms were involved was from the large thoraco-humeral muscles to the smaller forearm and hand muscles.* The trapezii seemed to be the first to contract, and this was followed almost at once by contraction of the deltoid and the remaining muscles of the shoulder girdle. Next followed spasm of the upper arm muscles, and finally those of the forearm and hand were involved. The spasm was at first tonic and resulted in adduction with slight flexion of the shoulder and slight flexion at the elbow and wrist with pronation of the forearm. The fingers were flexed at all joints and closed over the thumb, which was bent into the palm of the hand. In some attacks the left arm appeared to suffer more than the right. This tonic stage was rapidly replaced by clonic spasm of small range and brief duration. The lower extremities were unfortunately never very carefully observed, but the movement in them was never great. Spasm was felt in the thighs and in some attacks slight flexion of the hip and knee occurred. The position of the feet we are unable to describe owing to imperfect observation.

ON THE SUPPOSED REVERSAL OF THE LAW OF CONTRACTION IN DEGENERATED MUSCLE.

BY W. PAGE MAY, M.D., B.SC., F.R.C.P.
Fellow of University College.

(*From the Physiological Laboratory, University College, London.*)

THE law of contraction formulated by Pfluger, according to which excitation always occurs at the kathode at the make of a constant current, and at the anode at the break, has, except in the case of certain infusoria, where the size of the organism under investigation does not allow of a proper analysis of the conditions, been found to hold for all excitable tissues. The first experimental indication that the closing contraction is localised at the kathode was given by Schiff about half a century ago. The researches of physiologists have, moreover, rendered it extremely probable that the excitation at break is really due to the make of a polarisation current having its kathode at the former anode, and is, therefore, fundamentally of the same nature as the make contraction. We can only conceive of the excitatory effect produced by the passage of a current as being determined in some way by the electrolytic changes occurring at the points of entry and exit of the current from the excitable tissue. The development of cat-ions must, therefore, be associated or identical with the chemical changes which accompany or result in excitation. It is therefore extremely difficult to imagine that in the process of degeneration a sudden reversal of the fundamental chemical features of excitation should take place, and that excitation should now be associated with the development of an-ions. Yet this is supposed to occur, and is described as the *qualitative* reaction of degeneration. The well-known electrical changes obtained in the so-called reaction of degeneration are ably summarised in the classic work, "Diseases of the Nervous System," by Gowers and Taylor, and a short excerpt from the text, page 73, 3rd edition, is here given :—

"The changes we have hitherto considered are in the *degree* of irritability, 'quantitative' changes. But the quantitative increase in the muscular irritability is often accompanied by a change in the order of response, according to the pole that is applied and the strength of current—a 'qualitative' or 'polar' change. We have already considered its general characters, and have seen that it consists in an undue readiness of response at the positive pole (anode) compared with that at the negative pole (kathode), the muscle being normally the more sensitive to the latter. Writing Cl. for the closure of the circuit, O. for its opening, and C. for contraction, the normal reaction is—

$$\text{“(1) K.Cl.C.; (2)}\left\{\begin{array}{l}\text{An.Cl.C.;}\\ \text{An.O.C.;}\end{array}\right.\text{(3) K.O.C.}$$

"In disease—

$$\text{“(1)}\left\{\begin{array}{l}\text{K.Cl.C.;}\\ \text{An.Cl.C.;}\end{array}\right.\text{(2) An.O.C.; (3) K.O.C.: or even}$$

"(1) An.Cl.C.; (2) K.Cl.C.; (3) K.O.C.; (4) An.O.C.

"This qualitative change is at times absent, especially in cases of neuritis. It may be slight, and only amount to an equal kathodal and anodal excitability. It is practically constant when a nerve has been actually destroyed. On the other hand, it may be present and significant where less acute disease has not yet caused obtrusive wasting. Even when there is a marked quantitative change, the kathodal closure contraction may still occur first. When the change is present it is only in the muscles, and it must depend on the muscular fibres themselves. In the motor nerve the kathodal response is always the first, although a qualitative change has been detected in degenerated sensory nerves."

Bearing in mind how extremely difficult it often is, in clinical cases, to be certain of the results obtained, which frequently appear to contradict one another, there can be no question that, whereas in a normal muscle stimulated by the unipolar method contraction on the closing of the current always occurs first at the kathode, in a degenerated muscle the anodal closing contraction may not only occur far more readily than in the normal state, but far more readily than the kathodic closing contraction.

There is no doubt that this apparent reversal does take place in a large number of cases. If the reversal be other than apparent we should be face to face with a fact of enormous importance for all our conceptions underlying excitation and contraction. And it is surprising that the matter has not, before now, been put to the test of rigorous experiment. The only experiments of the sort with which I am acquainted are those carried out by Krehl ("Physiologische Pathologie," 1898, p. 537). This observer divided the lumbar plexus on one side in a number of frogs. In six to eight months the muscles were found to be in the state of granular degeneration which ensues, in a mammal, three to four weeks after nerve section. The sartorius muscle, which was much atrophied, was excised, and its behaviour on the passage of a current in the direction of its fibres investigated. No trace of reversal of the ordinary current effects was to be detected. The contraction, which was prolonged, began in every case at the kathode at make of the current, and at anode at break of the current. The behaviour of warm-blooded muscle was, however, not investigated.

In endeavouring to clear up this point on warm-blooded muscle, I was guided by the researches of Biedermann and his pupils on somewhat similar phenomena occurring in the unstriated muscle of the mammalian gut, and of the body-wall of certain worms. In these cases, also, on superficial observation, it might be said that the contraction of the circular muscles, on closure of a constant current, is anodic; whereas the longitudinal muscles appear to follow the ordinary laws of contraction. Biedermann found, however, that the apparent contraction at the anode of the circular muscles was really peri-polar. On using fine-pointed electrodes he found that, at the actual kathode, closure of the current caused a slight elevation, due to contraction of the fibres, which was surrounded by a more widely-spread area of depression and relaxation corresponding to the peri-polar zone. On the other hand, at the exact anode, there was a little dell caused by relaxation of the muscle, but surrounded by a circular ring of contraction in the peri-polar area. On loose observation only this peri-polar area had been noticed, and the contraction there had been regarded as an anodic closing contraction.

It seemed possible that a similar explanation might be found to hold for the apparent reversal of the law of contraction in degenerated muscle.

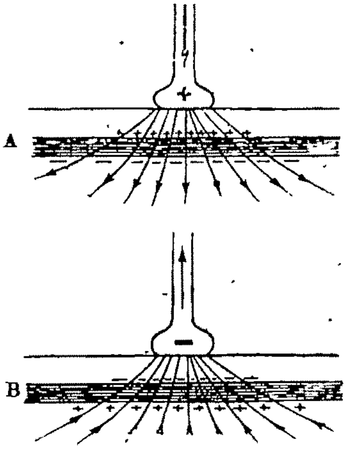


FIG. 1.

Electrodes applied to the skin over a nerve-trunk or muscle. In A the polar area is anelectrotonic and the peripolar katelectrotonic. The former condition therefore preponderates, since the current here is more concentrated. In B the conditions are reversed, the polar zone corresponding in this case to the kathode. (Waller.)

In the uni-polar method of excitation, which is the only method applicable to man, the current enters a few fibres at the anode, and thence spreads in all directions through the muscle. Every muscle fibre, therefore, will have anodic and kathodic points, but as the current is constantly spreading, the kathodic points will be more diffused than the anodic points (fig. 1, A). And, given a certain rise in excitability, the wide-spread peri-polar kathodic excitation may be more easily observable than the very limited anodic relaxation or absence of effect. It was therefore necessary to obtain muscles in the state of degeneration and test their behaviour to the passage of the constant current, using both large electrodes as well as finely-pointed electrodes.

To this end in a number of rabbits a piece was cut out of the sciatic nerve at the sciatic notch. Later on, when degeneration was well established, the affected muscles were exposed under an anæsthetic, and their excitability tested in various ways. In all the rabbits the excitability of the muscles underwent the familiar quantitative changes—a primary increase in faradic excitability, followed by disappearance of faradic excitability, and a marked increase in galvanic excitability. Not all of them, however, showed the qualitative change, the so-called reversal of the law of contraction, on stimulation through the skin. The further investigation of the excitability of the muscles was only undertaken in those rabbits in which the reversal-effect was obtained in the intact animal, using the ordinary modes of stimulation employed by clinicians.

Of these I need quote only one or two.

Rabbit 5.—Left sciatic nerve divided in sciatic notch, July 15, 1901. July 25.—Muscles of the affected side showed a great rise of galvanic excitability as compared with the sound side, but K.C.C. was slightly more readily obtained than A.C C. On August 13 the condition of the muscles was very much the same; the galvanic excitability was, however, still more marked, and K.C.C. and A.C.C were approximately equal. Under an anæsthetic, the semimembranosus was exposed, and its excitability tested by the unipolar method. The exciting current was derived from one storage cell, with a rheocord 250 cm. long. The units of current given corresponded to the centimetres on the rheocord. The muscle was first tested, using a broad brush moistened with normal saline clay as the exciting electrode, the indifferent electrode being applied to a small incision in the back of the neck. With the broad brush A.C.C. was obtained with 23 units of current; K.C.C. with 30 units, *i.e.*, reversal of the law of contraction. On using a finely-pointed electrode, and observing carefully the fibres immediately touched by the point, K.C.C. was obtained at 6 units, and A.C.C. at 9 units. The reversal of the law, therefore, was only apparent. This conclusion was confirmed by the results of exciting the excised muscle by means of two finely-pointed electrodes applied at different points of the muscle. It was then quite confined to the immediate neighbourhood of the kathode, using normal stimulation.

The same result was obtained in another rabbit, in which, on normal stimulation with electrodes applied to the skin, K.C.C. and A.C.C. had been found to be approximately equal. On stimulating the belly of the degenerated gastrocnemius with a large brush electrode, A.C.C. was obtained at 12 units, and K.C.C. with 14 units. On then replacing the brush electrode by a fine moistened thread, K.C.C. was obtained at 10 units, and A.C.C. at 23 units. This result was obtained many times, and we could only conclude that the reversal of the law of contraction in degenerating muscle, like the similar phenomena observed in the intestinal muscle, is only apparent, and dependent on the greater extension of peri-polar effects as compared with the polar.

A similar conclusion was arrived at as a result of recording the contractions of degenerated muscle. The normal response of such a muscle to the passage of a constant current is a prolonged chronic contraction at the kathode, an exaggeration, that is to say, of an effect which, by careful observation, can be detected even in a normal frog's muscle. Now, it is evident that when we are recording the contraction of a whole muscle, the prolonged contraction which occurs at the kathode will be more pronounced the greater the number of fibres in which the kathodic effect predominates. Using unipolar stimulation, therefore, we should expect to get the tonic contraction better marked on the record of the contraction of the whole muscle when the kathodic effect is widespread than when it is limited to one spot. When the kathode is applied to the muscle and the anode to some other part of the body, the kathodic effect is limited to the immediate neighbourhood of the kathode.

On the other hand, when the anode is applied to the muscle, the kathodes will be peripolar, and will be widely diffused throughout the muscle. Hence we should expect to get the tonic contraction more marked with a so-called anodal closing contraction than with a kathodal closing contraction —a condition which is well-marked in the curves reproduced in the figure.

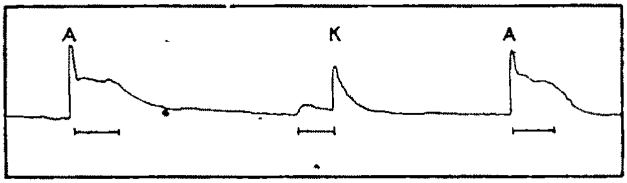


FIG. 2.

Tracings taken by attaching the tendon of the soleus of the rabbit, 30 days after section of the sciatic nerve, to the lever of a myograph. At A, K and A a constant current was passed through the muscle, one electrode being attached to the back of the neck, the other, a moistened thread, resting on the belly of the muscle. In A A, the muscle electrode was the anode, in K it was the kathode.

We may conclude, therefore, that Pflüger's law of contraction, according to which excitation occurs only at the point where the current is leaving the excitable tissue, is as true for degenerated muscle as for all other excitable tissues, and that the reversal of the law described by clinicians is only apparent, and determined by the special imperfect modes of testing which have been in use.

I am deeply indebted to Professor Starling for his ever ready help and criticism, and also for verifying the results of experiment described in the text.

INTERNAL HYDROCEPHALUS IN THE ADULT, WITH REMARKS ON THE ÆTIOLOGY OF HYDROCEPHALUS AND ITS OCCASIONAL ASSOCIATION WITH OTHER ABNORMAL CONDITIONS OF THE CENTRAL NERVOUS SYSTEM.

BY F. PARKES WEBER, M.D., F.R.C.P., LONDON,
Physician to the German Hospital.

A THIN and rather delicate-looking young woman, B.S., aged 22, single, a native of Saxony, was admitted into the German Hospital, June 10, 1901. She had already been ill about nine or ten weeks, suffering from headache, giddiness, and recurrent vomiting, and had been treated for gastric disorder.

Past History.—She was always healthy as a child. She was not subject to headache, and although she seldom took alcoholic stimulants, there was no evidence that alcohol affected her in any unusual way. No history of temporary deafness. She had twice suffered from erysipelas of the head. The first time was in her seventeenth year, and after the illness for a time she lost all the hair of her head. The second attack was a few years ago. During this she suffered from headache, and was kept three months in a hospital in Hanover. Afterwards she seemed well again. It is worth mentioning, however, that in the spring of 1901, when crossing from Hamburg to London, with the sea-sickness she seems to have lost, or almost lost, consciousness, being in a condition perhaps resembling the rare swooning form of *mal de mer,* and possibly suggesting the presence of some hitherto latent disease.

In the German Hospital examination of the gastric contents was reported to show absence of free hydrochloric acid and presence of lactic acid. When, however, the patient had been some time under observation the character of the vomiting was found to suggest a nervous origin. An attack would come on suddenly without accompanying gastric discomfort, especially after sudden movements. By ophthalmoscopic examination (July 15, 1901) distinct but slight optic neuritis was found in both eyes (on the right side more than the left). Stiffness in the cervical region of the spine was complained of soon after admission, at one time suggesting caries in the upper cervical vertebræ. The stiffness was more marked for rotation than for flexion of the head. There was no evidence of disease in the thoracic or abdominal organs, excepting the gastric disorder noted above. The patient did not seem to be hysterical. She was decidedly intelligent and quick at understanding, and could sing. There was no evidence of syphilis, either congenital or acquired. With the exception once or twice of an evening temperature of 100°F. fever was absent throughout.

Mercurial inunction was tried with doubtful result. The patient, however, gradually improved; the cervical rigidity completely disappeared, and she was able to be up and get about in the ward and was thinking of leaving the hospital.

In November the patient's troubles to some extent returned, and mercurial inunction was tried again. Pepsin was likewise given to aid digestion. Dr. Leonard Williams, who kindly took charge of the case during my absence, found her complaining of headache, vomiting and weakness. There was slight nystagmus on extreme lateral deviation, which was ill sustained. Optic neuritis in both eyes. The knee jerks were present, equal, and active. No clonus. The plantar reflex was of the flexor type. Dr. Williams found slight ataxia in one of the upper limbs. Vertigo was not a very prominent symptom of the case, but the sister of the ward says the patient on lying down after a bath would sometimes feel giddy and then suddenly vomit. Her gait was hesitating, rather that of a weak person taking small steps than that of a patient with cerebellar tumour or tabes. Deafness was not a symptom in the case.[1] Neither was there any mental disturbance such as occurs in general paralysis, nor any form of insanity such as has been observed in some cases.[2] On December 7, 1901, at about 6.30 a.m., the patient was suddenly seized with violent vomiting and frightful headache, and this was followed by general rigidity and clonic convulsive movements, death occurring about 7 30 a m. The pulse during the seizure was infrequent but regular, and the face was flushed at the end.

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[1] As it was in Hilton's case and in that of Burr and McCarthy, both of which I have quoted later on.

[2] See Burr and McCarthy's case quoted later on. See also Dr. T Whipham's account of a man, aged 39, with hydrocephalus and insanity (*Trans. Clinical Soc of London*, 1884, vol 17, p. 191) Dr. Whipham's case was not merely one of passive hydrocephalus or "hydrocephalus ex vacuo," as there was flattening of convolutions over a portion of the brain.

At the *post-mortem examination* the cerebral convolutions were found much flattened, and all the ventricles of the brain much distended with clear fluid, which spurted out when the ventricles were punctured, and was evidently under considerable tension. There was no evidence of thrombosis or any disease of vessels. No meningitis or thickening of the membranes discovered; no adhesions of pia-arachnoid to the dura mater; no disease of the bones of the skull or upper cervical vertebræ. The weight of the brain was excessive (1,588 grammes[1]—*i.e.*, 56 ounces—after being some time in formalin), but by macroscopic examination it showed nothing abnormal except an apparent thickening of the ependyma, which was most noticeable in the 4th ventricle. The choroid plexuses seemed healthy. The spinal cord was not examined. The stomach was not dilated, and there was no gastric ulcer or pyloric stenosis. Nothing noteworthy was discovered in the liver, kidneys, and the rest of the body.

Microscopic examination of the brain.—The upper part of the left ascending frontal convolution, part of the base of the brain, including a portion of the iter a tertio ad quartum ventriculum, part of the floor of the 4th ventricle close to the iter, and part of the medulla oblongata were examined. Sections were stained by the Weigert-Pal, Marchi, and Nissl methods. Sections of the ependyma from one of the lateral ventricles, from the third ventricle, and from different parts of the fourth ventricle were likewise examined, as well as a section of the choroid plexus of one of the lateral ventricles. All these sections were stained with logwood. The central canal of the medulla oblongata was, as it so often is, filled up with cells. The convolution showed nothing abnormal, unless, as Dr. F. E. Batten thought, slight "spacing of the nerve elements." The chief change was found in the ependyma of the fourth ventricle. The ependyma was infiltrated with round cells (fig. 1), and there was marked perivascular cell infiltration in the sub-ependy-

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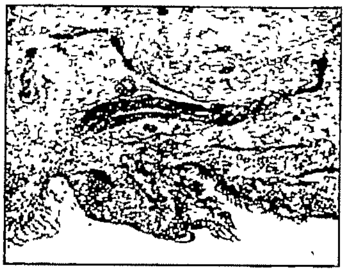
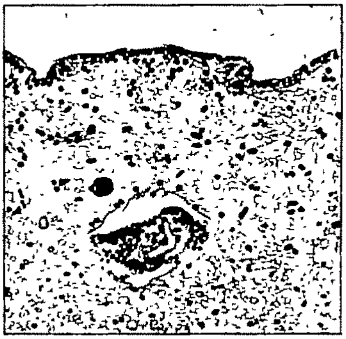
[1] This weight is decidedly excessive for a person of the patient's size, but it must not be considered very extraordinary. The brains of some notable men have weighed much more. Cuvier's is reported to have weighed almost 1,883 grammes (but see later footnote).



× 55 ½ Obj.

FIG. 1.

Section from floor of fourth ventricle, stained with hæmatoxylin. Ependymal surface rough and folded. No distinct epithelium at parts. Much cell-infiltration of the surface portion and around a sub-ependymal vessel (cut obliquely).



× 140 ¼ Obj.

FIG. 2.

A portion of the ependyma which is nearly normal (to compare with Fig. 1). Some perivascular cell-infiltration is however present—in the centre of the figure.

mal tissue. This inflammatory change was equally present near the iter and at the calamus scriptorius end, and was specially marked on the ependymal side of the membranous roof of the fourth ventricle and at the angle between the floor and roof. Sections from the ependyma of the third and lateral ventricles showed very much less change of this nature, the epithelium itself appearing nearly normal, though there was a little perivascular infiltration in the subjacent tissue. The section of the choroid plexus showed nothing very abnormal. A moderate number of the usual, more or less concentrically-marked, hyaloid or calcareous bodies could be seen, deeply stained with the hæmatoxylin; and at one spot the epithelium of the capsule appeared thickened and infiltrated. The changes revealed by microscopic examination might therefore be almost summed up as *ependymitis of the fourth ventricle.* I must take this opportunity of thanking Dr. Batten for his help in the examination of the brain and microscopic specimens.

I have convinced myself that apparent thickening or slight granulation of the ependyma in cases of hydrocephalus should not, by itself, be accepted as evidence of a genuine inflammatory process. One must remember that the whole ependyma has been subjected to chronic stretching. The pressure exerted by the serous effusion must, of necessity, damage the tissues immediately bordering the ventricles, and will probably cause necrosis of individual cells. In chronic cases a reactive change will follow and will be accompanied by a certain amount of cell infiltration, as it is everywhere when a local necrosis occurs (*e.g.*, the changes around anæmic infarcts in the kidney[1]). Moreover, the macroscopic appearance of thickening, as well as the microscopic appearance of cell infiltration, will both be intensified by the collapse of membranous parts when the cerebro-spinal fluid is let out, and by the shrinking due to the action of hardening reagents.[2] In the present case, however, there can be no doubt of the presence of true inflammatory changes in parts of the ependyma and sub-ependymal tissues. Moreover, the changes exactly resemble those figured by Burr and McCarthy as having been found in their case (to which I shall later on return), and as having been produced experimentally by the injection of irritating substances into the cerebral ventricles of cats.

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[1] I think the cirrhotic changes in the liver resulting from obstruction of bile ducts by ligature or gall-stones can be likewise *partially* explained as a reaction to a great distension of the ducts.

[2] In the same way an apparent thickening and cell accumulation in the intima of blood-vessels may be produced by the hardening reagents employed in preparing the specimens for microscopic examination.

The foregoing case is, in the main, similar to a case which I had the opportunity of seeing in Sir Dyce Duckworth's wards when acting as one of his medical clerks in 1887, and which he has kindly allowed me to refer to. The patient, a woman (A. S.) aged 57, suffered a considerable time, chiefly from severe headache, and had double optic neuritis. The necropsy ultimately showed the presence of simple internal hydrocephalus.

An apparently much more acute case than either of these was the following:—The patient, R. D., aged 21, a tailoress, born in Russia, was admitted on my side at the German Hospital in June, 1898. Eight days before admission she began to suffer from headache and attacks of vomiting. The headache was at first frontal and then occipital. She gradually became weaker, and just before admission had retention of urine. The general practitioner who had her sent to the hospital suspected a cerebral abscess. On admission, the pupils were found not to react to light and to be very small (pressure on the medulla?[1]) There was cervical rigidity. Temperature 98·8°F.; pulse 84, slightly irregular. Knee jerks natural. Urine, specific gravity 1020, no albumen or sugar. The patient died shortly after admission. At the necropsy the ventricles of the brain were found distended with clear fluid and the convolutions were flattened. There was slight thickening of the pia-arachnoid at the base of the brain, but nothing distinctly abnormal could be found. The lining of the lateral ventricles appeared slightly granular, but a microscopic examination showed nothing noteworthy. No disease was found in the heart, lungs, &c.

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[1] Generally in adults with chronic hydrocephalus the tendency has been for the pupils to be dilated.

This case[1] may fairly be considered an example of acute internal hydrocephalus, similar to some of those described by Quincke and others, apparently resulting from serous meningitis.

Apart from what may be termed "passive hydrocephalus," "hydrocephalus ex vacuo,"[2] or "hydrops cerebralis ex vacuo," in which a portion or the whole of one or more of the ventricles is enlarged owing to some atrophic[3] condition of the neighbouring parts of the brain, cases of internal hydrocephalus may be divided into the following groups, the grouping being rather for convenience than for pathological correctness.

(1) Cases secondary to and a part of the phenomena of tuberculous[4] or any suppurative meningitis.

(2) Cases resulting from the presence of tumours, parasites, caseous nodules, abscesses, inflammatory foci, &c.[5]

(3) Traumatic cases.

(4) Cases of ordinary infantile or congenital hydrocephalus, whether or not associated with inflammatory thickening of the membranous roof of the fourth ventricle, involving Magendie's and the other foramina in it.

(5) Cases of internal hydrocephalus supervening on (or during convalescence from) epidemic or sporadic cerebrospinal (non-suppurative) meningitis. Of this group many typical examples have been recorded. Dr. E. P. Joslin,[6]

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[1] Which I have already described in a paper in *St. Bart. Hosp. Reports*, vol. 34, p. 307.

[2] This so-called *hydrocephalus ex vacuo* may certainly be internal, and therefore is not merely synonymous with *hydrocephalus externus*, as Osler ("Principles and Practice of Medicine," 1901, fourth edition, p. 1028) gives it.

[3] The atrophy may be due to various causes. In certain cases there may at one time have been active internal hydrocephalus, and the pressure of the intra-ventricular effusion may have subsequently subsided.

[4] In some standard text-books and dictionaries the term "Acute hydrocephalus" is still given as synonymous with tuberculous meningitis, but this is altogether unjustified in the light of modern data on the subject.

[5] This class would include certain cases labelled "Meningitis serosa acuta," in which the exudation has not yet had time to become purulent, secondary to ear disease, &c. Compare Dr. J. Hegener, "Beitrag zur Lehre von der Meningitis serosa acuta," *Muenchener Med. Wochenschr*, 1901, No. 16, p. 617.

[6] *American Journal Medical Sciences*, October, 1900, pp 444-468.

who gives an excellent account of the literature of the subject, says internal hydrocephalus has been known to be a result of epidemic cerebro-spinal meningitis since 1805, the year in which the disease is usually considered first to have appeared.

(6) Cases of so-called simple or idiopathic internal hydrocephalus of adults and older children due to a non-suppurative (serous) ependymitis or ventricular meningitis. See H. Quincke,[1] Gowers,[2] A. Heidenhain,[3] &c., on this subject.

A typical example of the so-called ventricular meningitis would seem to be the case described by Drs. C. W. Burr and D. J. McCarthy.[4] The patient, a male, aged 33, was suddenly seized with fever, cervical rigidity, headache, stupor and delirium. The fever fluctuated between 101° and 103.4° F. After three weeks, during which the intensity of the symptoms varied greatly, he improved much physically, but he was weak and his mental state was peculiar; he was altogether unlike his usual self, seeming rather like a man in the beginning stage of general paralysis. A week later the fever and meningeal symptoms returned, lasting about a week. Then after four days' interval they returned again and ended in death. *Post-mortem* examination revealed only a moderate internal hydrocephalus, proliferation of the ependyma and ependymal glia, perivascular round-cell infiltration in the sub-ependymal tissues, and sclerotic and degenerative changes in the choroid plexus. The authors give good plates of the changes observed and compare them to the changes produced by the injection of hydrochloric acid (five per cent.) or of sterile urine into the cerebral ventricles of cats.

My case (B. S.) belongs doubtless to this group, and the changes seen in the microscopic sections of the floor of the fourth ventricle correspond exactly to the changes in the ependyma and subependymal tissues described and illustrated by Burr and McCarthy in their case.

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[1] Publications referred to later on.

[2] "Diseases of the Nervous System," 1893, vol. 2, p. 584.

[3] "Hydrocephalus acutus acquisitus internus," *Berliner med. Wochenschr.*, 1899, No. 49, p. 1078.

[4] *Journal of Experimental Medicine*, 1900, vol. 5, p. 195.

The whole subject of hydrocephalus and effusions into the ventricles can, I think, best be understood by comparison with effusions into the pleura or peritoneum. My first group corresponds to pleuritic effusions due to tuberculosis, or septic infection of the pleura. The second group is analogous to pleuritic effusions accompanying tumours, &c., close to or involving the pleura. The third group, traumatic hydrocephalus, seems hardly analogous to the results of injury to the thorax, though some cases may probably be compared to traumatic pleuritic effusions, containing blood mixed with serous fluid, following injury and bruising of the chest walls and lungs.[1] Chronic alterations in the walls of the cerebral vessels, due to chronic alcoholism, renal disease, &c., would doubtless sometimes play a part in the production of such traumatic cases. Perhaps, however, trauma should merely be considered as a possible exciting cause of hydrocephalus in children and adults, rather than as a basis for making a special group of cases (" traumatic "). Whatever the connection between trauma and hydrocephalus may generally be, there can be no doubt that a blow on the head has been the starting point of the symptoms in several well-recorded cases.

I shall now confine myself to the remaining three groups (4 to 6), and when speaking of internal hydrocephalus during the rest of the paper, my remarks should be understood as referring to these groups only. All the cases (excepting perhaps certain cases of infantile and congenital hydrocephalus, in which no evidence of previous posterior basal meningitis is found at the necropsy [2]) may be compared, I think, to non-suppurative pleuritis, that is, to pleuritis with serous effusion. The cases supervening on epidemic cerebrospinal meningitis (group 5) only differ from groups 4 and 6 in their connection with an epidemic disease, and therefore in their direct or indirect relation to the specific microbic cause of the epidemic; but some cases of groups 4 and 6 are perhaps really cases following "sporadic" cerebro-spinal meningitis.[1] Between groups 4 (at least the cases showing signs of past meningitis) and 6 there is no clear pathogenic difference. Infancy is the favourite period for hydrocephalus to commence, and therefore far more cases fall into group 4 than into group 6, and, owing to the easy yielding of the skull[2] and consequent enlargement of the head, the diagnosis is more readily made in early life. Moreover, as will afterwards be shown, many cases classed with group 6, may quite probably be instances of acute exacerbations of chronic (more or less latent) hydrocephalus or else recurrences of the disease in apparently cured patients.

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[1] Dr. J Fawcett (*Trans. Path. Soc.*, London, 1897, vol. xlviii., p. 6) records the case of a boy aged 12, and gives other evidence in support of the view that a blow on the head may cause laceration of the iter, and lead to its cicatricial stenosis and to internal hydrocephalus.

[2] *Cf.* Lees and Barlow, in Allbutt's "System of Medicine," vol. vii., p. 545.

Professor Heinrich Quincke[3] has recorded a number of cases of hydrocephalus in adults, both fatal cases in which a necropsy was made and cases in which recovery took place, but in which the diagnosis was made more or less probable by the symptoms observed. By his description of cases and his work on spinal puncture he has doubtless contributed more than anyone else towards elucidation of the subject. He has grouped all cases of cortical or ventricular meningitis with serous effusion under the heading "serous meningitis" (meningitis serosa), and, as this name implies, he originally considered the serous effusion to be inflammatory. More recently,[4] however, he has laid stress on the possibly angioneurotic origin of *some* cases, and Dr. W. Murrell[1] has likewise described a case which he believes to have been of angioneurotic nature.

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[1] For instance, in H. Oppenheim's case (*Charité-Annalen*, Berlin, 1890, Jahrgang xv., p. 307) of a female, who died at the age of about 27, from an exacerbation of internal hydrocephalus, the first symptoms of which dated from the eighteenth year, the necropsy showed distension of all the ventricles and thickening of the ependyma and of the pia mater under the third ventricle, whilst the pia mater of a considerable area of the spinal cord was slightly adherent to the dura mater.' So also in Eichhorst's case of a student, aged 28 (referred to in a later footnote), the membranes over the infundibulum of the brain were thickened, and the pia mater in the dorsal region of the cord was adherent to the dura mater.

[2] The head has, however, been known to increase in size from intracranial pressure after the time for closure of the sutures.

[3] See especially "Ueber Meningitis Serosa," in Volkmann's *Sammlung klinischer Vorträge*, Neue Folge, Innere Medicin, No. 23, 1893.

[4] See especially "Ueber Meningitis serosa und verwandte Zustände," by H. Quincke, *Deutsche Zeitschrift für Nervenheilkunde*, 1897, vol. ix., pp. 149-168.

This theory of an "angioneurotic hydrocephalus" seems to me, however—at least at present—to lack evidence to support it; and Quincke himself would probably only apply the angioneurotic theory to cases commencing suddenly without fever and of relatively short duration; analogous, in fact, to cases of angioneurotic œdema of the skin, and in which, perhaps, there might be an œdematous infiltration of the brain substance as well as an effusion into the ventricles.

Relatively high pressure of the intraventricular effusion is perhaps as consistent with the angioneurotic as with the inflammatory theory, but when the effusion of cerebro-spinal fluid is merely of angioneurotic origin, the specific gravity of the effused fluid and its richness in albumen should probably not be excessive. Following are a few records of the specific gravity of the cerebro-spinal fluid in cases of internal hydrocephalus. In a case of Quincke,[2] referred to in greater detail later on, the specific gravity of the fluid obtained by lumbar puncture was as high as 1015, and it contained a considerable amount of albumen. In a case related by Joslin[3] the fluid obtained at the necropsy showed a specific gravity of 1010, and contained one half per mille albumen. In a boy,[4] aged 8¾, apparently suffering from chronic hydrocephalus, the clear cerebro-spinal fluid obtained by lumbar puncture was of specific gravity 1008, and contained one half per mille albumen. In a boy[5] 9 years old, lumbar puncture gave a clear fluid of specific gravity 1008, containing three-quarters per mille albumen. In two hydrocephalic infants[6] the cerebro-spinal fluid obtained by lumbar puncture was, in the first case (from a spina bifida), of specific gravity 1007, with half per mille albumen; in the second case, of specific gravity 1009, with three-quarters per mille albumen. In seven other patients referred to by Quincke,[1] between 12 and 41 years of age, the cerebro-spinal fluid obtained by lumbar puncture had a specific gravity of 1007-1010, and contained one half to 2·7 per mille albumen.

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[1] *Lancet*, April 28, 1900, p. 1,206. Murrell uses the term, "Quincke's Disease," but surely, if used at all, this term should signify "Angioneurotic œdema of the skin," in connection with which Quincke's name is so well known.

[2] *Verhandlungen des X. Congresses für inn. Med*, Wiesbaden, 1891, p. 338.

[3] *Loc. cit.*, p. 449, Case iii.

[4] Quincke, Volkmann's *Sammlung*, *loc. cit.*, p. 664, Case 9.

[5] Quincke, Volkmann's *Sammlung*, *loc. cit.*, p. 666, Case 12.

[6] Quincke, Volkmann's *Sammlung*, *loc. cit.*, pp. 687-9, Cases 1 and 2. In the first case the fluid was obtained by tapping a spina bifida in the lumbar region, but at the necropsy the fluid distending the lateral ventricles was found shut off by occlusion of the iter. Recently I had the opportunity of examining the fluid obtained by tapping the lateral ventricle of an infant with ordinary chronic hydrocephalus. It was clear, of specific gravity 1005, giving a thin cloud of albumen and slightly reducing Fehling's solution.

On the whole, it is best to consider the angioneurotic theory of hydrocephalus as not well supported, and it is questionable whether the theory is required to account for any of the cases. For it must be remembered that only a limited portion of the ependyma and meninges need be inflamed to cause an effusion. The macroscopic appearance of thickening of the ependyma is not necessarily due to cell infiltration, and the presence or absence of this infiltration cannot be determined without microscopic examination. Thus, in my present case (B. S.) a portion of ependyma, examined microscopically, showed practical absence of cell infiltration, though it appeared thickened like the infiltrated portion. When there is a more or less general appearance of thickening or granulation of the ependyma, owing to shrinking after relief of the tension (due to escape of the cerebro-spinal fluid at the necropsy), the evidence of real inflammation might be overlooked, owing to a portion of the ependyma being selected for microscopic examination which happened not to show typical cell-infiltration. In Prof. H. Eichhort's[2] case of a student, aged 23, who, after an illness of a few months' duration, died with symptoms of cerebral compression, which the necropsy showed to be due to internal hydrocephalus, it is expressly stated that the ependyma was not universally much thickened, but in numerous small patches only. In some cases of localised ependymitis the effused fluid might even not be of particularly high specific gravity or particularly rich in albumen. For the fluid effused from the limited inflamed surface might have an irritating quality, leading to the copious pouring-out of normal, or nearly normal, cerebro-spinal fluid from the non-inflamed surfaces.[1] Moreover, local conditions of the circulation (venous and lymphatic obstruction, by pressure or otherwise, in the choroid plexuses and venæ Galeni) would doubtless influence the rapidity and pressure of the effusion and the quality of the fluid effused. Thus sudden changes in position of the patient's body, alcoholic stimulants, exposure to heat or cold, mental or physical exertion, would all exercise an influence. To the probable effect, in this respect, of closure of Magendie's foramen, I shall refer later on. General conditions, such as renal disease and chronic alcoholism, producing alterations in the blood and blood-vessels, would likewise, if present, have an influence on the effusion.

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[1] *Deut Zeit. f. Nervenheilkunde, loc cit.*, Cases 1, 2, 3, 4, 6, 8, 9.

[2] *Zeitschrift fur klin. Medicin*, Berlin, 1891, vol. xix., Supplement, p. 181.

The difficulties of the whole subject can best be exemplified by returning to the comparison with serous effusions into the pleura and peritoneum. Chance necropsies after attacks of pleuritis show that only limited portions of the pleura need be much affected. In fact, in serous pleuritis the inflammation may be very unequally distributed over the serous membrane, and a small portion only of the pleura need be inflamed to give rise to a serous effusion of the whole pleura. These circumstances by themselves, independently of important local and general conditions of the circulation, may account for much of the variation in the quality of the effused. fluid observed in cases of serous pleuritis.

Like many others, I think that ascites occurring in cases of early hepatic cirrhosis and cardiac disease is frequently entirely or partially due to inflammatory changes; but I believe that the reason why this has not been generally admitted is that the peritoneal inflammation in such cases (a serous peritonitis analogous to a serous pleuritis) is often limited to a very small area[2] only of the peritoneal surface, though it gives rise to a general ascitic effusion. If this be recognised and the influence of abnormal conditions of the general and local circulation be likewise considered, one cannot wonder that the specific gravity of the ascitic fluid in such cases may vary considerably, that it may be in some cases as high as 1016 to 1020, though in other cases it is only 1010 or 1012 or thereabouts. Yet I believe the specific gravity of the effused fluid may sometimes be helpful in recognising the inflammatory origin of such effusions, whether in the peritoneum, pleura or cavities of the central nervous system.

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[1] From a "teleologic" point of view, the fluid from the non-inflamed surfaces is poured out with the object of diluting the irritating fluid poured out from the inflamed surface.

[2] For instance, there may be only a little perihepatitis or perisplenitis, as I remarked at the discussion of Dr. Campbell Thomson's paper at the Royal Medical and Chirurgical Society (*Lancet*, June 15, 1901, p. 1686).

I come now to the question of the inflammatory closure of the foramen of Magendie and the neighbouring foramina in the roof of the fourth ventricle between the cerebellum and medulla, and to the possible influence of this closure (or of inflammatory thickening and consequently lessened permeability of the whole membranous roof of the fourth ventricle) in the pathogeny of internal hydrocephalus. *Post-mortem* observations show that thickening of this region is not invariably present in cases of internal hydrocephalus, and therefore the change in question cannot be regarded as the only essential factor in the pathogeny of the hydrocephalus. The reason why inflammatory thickening or "plastering" of the membranous roof of the fourth ventricle is almost invariably found *post mortem* in cases of internal hydrocephalus supervening on epidemic or sporadic cerebro-spinal meningitis, such as those described by Joslin,[1] is probably that the region is one of the sites of election in the kind of meningitis in question. It can scarcely be doubted, however, that the inflammatory thickening of this region, when present in any case, may be regarded as a factor in the production of the hydrocephalus, though of course it can have no influence in the rare cases in which the fourth ventricle is not involved in the hydrocephalic distention and in which there is obstruction in the iter[2] or closure of one of the lateral ventricles.[3]

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[1] *Loc. cit.*

[2] Blocking of the iter, doubtless sometimes congenital, may be due to tumours or parasites or inflammatory changes, or apparently to cicatricial stenosis resulting from traumatism, as in Dr. J. Fawcett's case (*loc. cit.*).

[3] E. Ziegler, *Lehrbuch der spec. Path. Anatomie.* Ninth edition, 1898, p. 832.

I have now to consider certain points of interest connected with internal hydrocephalus in adults and elder children, the first being the fact that, as Quincke has pointed out, apparently acute "idiopathic" cases are in reality sometimes only exacerbations of a chronic condition, which occasionally even dates from early childhood or infancy. As examples I will quote a few cases, and first of all the well known one described by John Hilton.[1]

A gentleman, who died at the age of 34. As a child he was active, but irritable in temper; as a man he was very spare and delicate looking. The terminal phalanges of his fingers were very short, and the nails inserted like seeds into the cuticle. He was fond of intellectual pursuits, and had a great dislike to excitement and noise. Excitement frequently brought on an impediment in his speech. At the age of 16 he had a severe nervous illness with depression, said to have been brought on by application to business in the City, which, however, was not of a kind to affect ordinary persons. Tea, coffee, and cocoa seemed to affect his head and derange his stomach, and he had an instinctive dislike to alcoholic stimulants of every kind. As he said himself, he only half lived in the winter; he seemed torpid, and would drop into a deep sleep after a meal, from which it was very difficult to rouse him at bedtime, when he seemed scarcely to know where he was. Though he was subject to coldness of the extremities, and though both winter and cold always affected him injuriously, yet he could not bear a warm room, as it made him feel faint. For many years he was subject to headache, derangement of stomach, and occasional deafness. His pulse was usually weak, irregular, and somewhat infrequent, about 50 to 60 beats in the minute A peculiar uneasy look of the eyes, with dilated pupils and muddiness of the conjunctiva, was said to be noticeable when his health was temporarily deranged. During the last year of his life he gradually lost flesh and became more feeble, acquiring a slight stoop in his gait. He also seemed to be affected with slight stiffness of the neck. A few months before his death he had a severe attack of vomiting, with prostration, without obvious cause. On the day of his death he had been out, about a mile or so, from home, and had twice been seized with vomiting. He walked home, but felt giddy and oppressed, and was placed on a bed. He died in a short time with stertorous breathing, although he remained sensible almost to the last moment. At the *necropsy* the cerebral convolutions were found flattened, and were rather large and few for the man's age, suggesting a certain degree of arrested development. The lateral ventricles contained at least four ounces of clear cerebro-spinal fluid. The fourth ventricle was greatly dilated in all its directions. The septum lucidum and fornix were softened, but the microscope showed no trace of inflammatory deposit. There was a tolerably dense membranous structure between the under surface of the cerebellum and the upper surface of the medulla oblongata, closing the cerebro-spinal aperture and forming a kind of pouch projecting downwards, thus showing the direction of the fluid tension upon it to have been from above downwards. Hilton concluded that the gastric trouble and occasional deafness were due to distension of the fourth ventricle, with consequent pressure on the origins of the pneumogastric and auditory nerves.[1] "His brain could bear no fulness of blood, no increase of size, because the cerebro-spinal fluid could not escape from the interior of the brain. He could not take wine, beer, or spirits;[2] and could bear no muscular exertion. The congestion of the brain produced vomiting by pressure upon the medulla oblongata, exerting its influence through the pneumogastric nerve."

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[1] "Influence of Mechanical and Physiological Rest." First edition, London, 1863, p. 39. Some points in this history suggest that the patient may have had syringomyelia as well as hydrocephalus.

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[1] In Burr and McCarthy's case, already alluded to, deafness was one of the symptoms, and, *post mortem*, the eighth pair of cranial nerves were found very much degenerated.

[2] Compare this case with the case recorded by F. Plehn (quoted by H. Quincke, Volkmann's *Sammlung*, *loc. cit.*, p. 670). A student ever since his tenth year, when he was rendered unconscious by a fall, suffered every three to eight days from attacks of severe headache, lasting several hours. Speaking or the application of cold to the head during the attacks made them worse, and he was very careful in regard to alcohol, owing to its increasing his headaches. At the age of 23, after spending an evening with his friends, he was seized with a worse headache than usual, followed by loss of consciousness, Cheyne-Stokes breathing, and death. The necropsy showed distension and dilatation of all four cerebral ventricles, and thickened ependyma. There was a sacculated dilatation of the fourth ventricle at the point of the calamus scriptorious. The pia mater was thickened over the posterior part of the cerebellum, and the foramen of Magendie seemed to be obliterated. Fagge (see Fagge and Pye-Smith, "Medicine," 1901, vol. i., p. 883) recorded the case of a bank porter whose symptoms had commenced seven years previously, after a blow on the head. Ever since the injury he had been liable to attacks of occipital pain and vertigo; reading often made him feel giddy, and he could scarcely take any stimulant.

The next case I have selected is one recorded by Professor H. Quincke[1] at the German Medical Congress at Wiesbaden, in 1891.

The patient was a man, aged 25, who had often suffered from headache since December, 1889, and from vertigo since the spring of 1890; in the following June optic neuritis was noted. There was no history of previous illness, but the least indulgence in alcohol or tobacco had always made him feel giddy. On admission into the hospital, November 7, 1890, the patient, a strongly-built, big man, suffered from headache and vertigo. Both eyelids were moderately swollen. Optic neuritis. No paralysis of limbs. The diagnosis rested between cerebral tumour, chronic meningitis, and exacerbation of an old hydrocephalus. Ice-bags, purgatives, iodide of potassium and mercury had no thorough effect, though the headache almost went away, and at times the vertigo was much diminished. Counter-irritation gave some relief. On April 3, 1891, the cerebro-spinal fluid was tapped by lumbar puncture, the manometer pressure being 50 cm. water, equal to 37 mm. mercury. In the course of an hour 80 cc. of clear fluid came away, of specific gravity 1015, containing a considerable amount of albumen. On the following day there was less vertigo.

Quincke regards the case as an exacerbation of a hitherto latent chronic hydrocephalus, and it seems to me that the character of the cerebro-spinal fluid removed by spinal puncture throws light upon the nature of the exacerbations in such cases.

The following case, recorded by Dr. Frederick Taylor,[2] is instructive, because the patient, who died from an exacerbation of chronic hydrocephalus at the age of 16, seemed to show signs of congenital hydrocephalus by the large size of his head at birth. It is unfortunate that the weight of the brain at death is neither mentioned in this nor in Hilton's case; both the patients in question gave evidence of considerable intellectual development, and possibly had slightly "hypertrophied" brains, such as those alluded to later on.

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[1] *Verhandlung des X. Congresses fur innere Medicin*, Wiesbaden, 1891, p. 333. This case may be compared to some of those described by Quincke in Volkmann's *Sammlung*, *loc. cit*, and in the *Deut. Zeit. fur Nervenheilkunde*, *loc. cit.*

[2] *Transactions of the Clinical Society of London*, 1897, vol. xxx., p. 175

Dr. Taylor's patient was a boy aged 16, admitted into Guy's Hospital, September 11, 1895. His head was large from birth. At 8 months he had bronchitis and fits. He did not walk properly till he was 1 year and 10 months old. He talked plainly at 2½. At 8 he had scarlatina, which was followed by nocturnal incontinence of urine. At 12 he learned the violin, and could play it and sing well. At 13½ he left school, and became a compositor, working regularly about 54 hours a week. His mother considered him to be strong and active, and quick at picking up information. Headache and vomiting were the prominent symptoms in the hospital. Headache had been first complained of in August, 1895, and vomiting on September 2. His gait was unsteady. There was no anæsthesia or loss of sensibility to pain or temperature. Knee-jerks somewhat increased on both sides. Optic discs normal. The headache was constant across the forehead, and occasional over the occiput, sometimes very severe, especially on sitting up. On September 16 the head was retracted, and during the next days patient was drowsy. On September 19 there was severe pain in the back of the neck. Weakness in legs. On September 20 there was a little fever. Weakness in all limbs; increasing in the legs. Knee-jerks absent. Slightly drowsy. Speech hesitating. Some nystagmus. No optic neuritis. Embarrassed breathing. Cyanosis. Death. At the necropsy the bones of the skull were found to be remarkably thinned by pressure. The pia arachnoid was thickened over the base of the cerebellum, particularly near the foramen of Magendie. It was adherent to the dura mater in several places, especially over the foramen magnum. There were thirty ounces of liquid in the distended ventricles. The ependyma was granular.

Occasionally hydrocephalic patients, with heads already greatly enlarged in childhood, have lived to adult life. A well-known example of this is the man James Cardinal, the subject of chronic hydrocephalus from infancy, who died at Guy's Hospital in 1825 at the age of nearly 30 years, probably of some different disease.[1] It is very probable that some of the persons who have been celebrated on account of the excessively large size of their heads are analogous examples. M. A. Ruffer[2] refers to cases in which a considerably greater age than that of Cardinal was attained. Dr. W. A. Brailey's case[3] was a woman who died of acute pneumonia at the age of 53; and Trousseau[4] mentions two old men, aged 72 and 78 respectively, whose history was known to Frank, and who were hydrocephalic from birth.

Though in my present case (B. S.) there is no history pointing to the early presence of hydrocephalus, as there is in some of the cases I have just quoted, yet the overgrowth of the brain, shown by its weight, points to the fatal illness being probably a complication of a much older disease. It brings the case into connection with those of the so called "hypertrophy of the brain," or "megalencephaly," an excellent example of which was shown in 1900 to the Pathological Society of London by Dr. H. Morley Fletcher.[5] L. Edinger[6] says that his friend Perls first conjectured that the pressure exerted on the brain by the skull might be reduced in cases of hydrocephalus which are undergoing cure, and that the brain substance might, as a result of not being opposed by the normal pressure of the skull, increase abnormally in bulk.

One may suppose that if this conjecture be correct, and if such increase be due merely to overgrowth of the connective tissue elements, it may lead to mental backwardness or defective intelligence and to imbeciles with heavy brains; but if the nobler elements participate equally in the excessive growth unusual intellectual powers may, as Perls and Edinger have suggested, be the result. In my case (B. S.) there may have been a hydrocephalic tendency in early life, the brain afterwards undergoing abnormal increase in size[1] as a consequence of recovery. The later disease may have been a recurrence started by the second attack of erysipelas.

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[1] Possibly of pulmonary and intestinal tuberculosis. See the account given of Cardinal's case by Dr. Richard Bright, *Reports of Medical Cases*, London, 1831, vol. ii., p. 431.

[2] "Critical Digest on Chronic Hydrocephalus," BRAIN, 1890, vol. xiii., p. 251.

[3] *Trans. Path. Soc. of London*, 1881, vol. xxxii., p. 1.

[4] "Clinical Medicine," New Sydenham Society's Translation, London, 1868, vol. i., p. 475.

[5] "A case of Megalencephaly," *Trans. Path. Soc., London*, 1900, vol. 51, p. 230.

[6] "The Anatomy of the Central Nervous System," English translation, by Dr. W. S. Hall, 1899, p. 206.

There are cases of internal hydrocephalus in elder children or adults in which *post-mortem* examination has demonstrated that a condition of hydromyelia or syringomyelia of the spinal cord has likewise been present. Dr. Pierre Marie[2] recorded the case of a man, who died at the age of 36, in whom at the *post-mortem* examination a condition of hydrocephalus was found associated with extensive hydromyelia or syringomyelia of the cord. I have likewise heard of two cases of fatal hydrocephalus, in which at the necropsy the presence of syringomyelia or hydromyelia in some part of the spinal cord was ascertained. In the same way hydrocephalus in infants has long been[3] recognised as not rarely associated with spina bifida, a congenital abnormality certainly to some extent allied to hydromyelia and syringomyelia, even though the last mentioned condition can hardly be termed congenital.[4]

The foregoing considerations all lead one to suspect that some of the cases described as "idiopathic" acute internal hydrocephalus in adults (the *post-mortem* examinations being often only partial) may in reality have been exacerbations in chronic cases, or at least connected with old abnormal conditions of the central nervous system.

I now come to another matter, namely, the rare occurrence of symptoms of internal hydrocephalus in persons with a myxœdema-like puffiness or œdema of the face. When a student, in 1887, I saw a young man, aged 18, who died at the German Hospital with internal hydrocephalus, the *post-mortem* examination showing no other cerebral disease except distension of the ventricles with cerebrospinal fluid. The puffiness of the skin in his case was so remarkable that the diagnosis of myxœdema had been made by a great authority on the subject. In Quincke's case, of which I have already given an abstract, the eyelids are stated to have appeared swollen. I should have regarded the myxœdema-like condition in the young man as a coincidence, were it not that I afterwards read Quincke's paper, and that in November, 1900, my colleague, Dr. zum Busch, kindly showed me a small child, under his care at the German Hospital, in whom a striking myxœdema-like puffiness of the face was noted, together with symptoms of cerebral compression, supposed to have followed an injury. The cerebral symptoms improved after spinal puncture. Whatever the explanation of these facts may be, it must be admitted that the occasional facial œdema and the exciting influence of traumatism lends some, though I think insufficient, support to the theory of the existence of an angioneurotic hydrocephalus. In this connection I may likewise draw attention to certain cases in which a chronic condition of solid œdema about the eyelids and face is associated with recurrent erysipelas-like attacks. My patient (B. S.) was stated to have suffered previously from erysipelas; and in a girl, aged 14, whose case is described by Quincke,[1] the cerebral symptoms commenced after an attack of facial erysipelas, though the relatively large head of the patient suggested the possibility of previous latent chronic hydrocephalus.

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[1] It is unfortunate that we have not more records of the weights of hydrocephalic brains from patients of various ages. Hervé suggested that Cuvier was affected with hydrocephalus in his childhood. At the *post-mortem* examination it was found that the lateral ventricles were very large. According to E. Rousseau's account the weight of his brain was 1861·2 grammes, but according to Bérard's official report it was still greater, 1882 9 grammes. (See *Revue de Thérapeutique*, Paris, December, 1883, page 623.)

[2] Société de Neurologie, Paris, December 7, 1899.

[3] See Dr. Richard Bright, *op. cit.*, vol. 2, p. 428.

[4] See however H. Schlesinger's classification (*Syringomyelia*, 1902).

The *chief symptoms* of hydrocephalus in adults appear to be: headache, stiffness in the neck, sudden violent attacks of vomiting, double optic neuritis, weakness, and a hesitating gait. In the present case the changes shown by ophthalmoscopic examination were not very great, but in the case of a labourer, aged 31, recorded by Annuske,[1] in which death occurred after an illness of about five months, and in which the necropsy showed great dilatation of all the ventricles, blindness was complete in about three months. Some of the cases which recover show quite as marked ophthalmoscopic changes as fatal cases do; for instance, in a woman, aged 22, recovery from the brain symptoms took place after ten months, but was accompanied by amaurosis due to optic nerve atrophy.[2] In some of the necropsies the floor of the third ventricle and the infundibulum have been found much bulged out by the hydrocephalic effusion, showing the special pressure to which the optic tracts and the optic chiasma must have been subjected. In Taylor's case, however, to which I have already referred, there was no optic neuritis, even shortly before the patient's death. Other cranial nerves beside the optic are sometimes affected. Thus, in Hilton's case and that of Burr and McCarthy, both already referred to, the auditory nerves suffered; in a young woman, the subject of a paper by Oppenheim,[3] there was complete anosmia, and at the necropsy the olfactory nerves were found much flattened out.

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[1] Volkmann's *Sammlung*, *loc. cit.*, p. 659, Case 4

The vomiting was sometimes very violent in the present case. A notable feature was the tendency to vomit on lying down after being in the upright position. This effect of lying down suddenly may be accounted for if we remember that the change of position favours the flow of blood to the head, and thus adds to the pressure, due to the hydrocephalic effusion, to which the brain is already subjected. Some of the symptoms noted in Hilton's case may be compared to it. Oppenheim on one occasion, in the case to which I have just referred, noted that the patient continually held her head forwards and to the left, because attempting to move it to the contrary position immediately induced vomiting.

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[1] von Graafe's *Arch. f. Ophthalmologie*, Berlin, 1873, vol. xix., Part III. p. 260, Case 6. It is quoted by Quincke, Volkmann's *Sammlung*, *loc. cit.*, p. 669.

[2] Quincke, *Deut. Zeit. f. Nervenheilkunde*, *loc. cit.*, p. 150, Case 2.

[3] The case (*Charité-Annalen*, *loc. cit.*) has already been quoted in a footnote.

Before the onset of the cervical rigidity, the vomiting in the patient, B. S., was supposed to be due to gastric disease. Fagge,[1] amongst various cases of adult hydrocephalus at Guy's Hospital, mentions that of a man aged 55, who had complained of severe pains in the head three months before his death, and was admitted into the hospital for symptoms resembling those of chronic dilatation of the stomach. He died in a semi-comatose condition a few hours after a convulsion. Strauss[2] mentions the case of a man aged 50, who died with symptoms resembling those of cancer of the œsophagus. At the necropsy nothing could be found to account for the œsophageal obstruction, but chronic internal hydrocephalus was present. During life, however, there had certainly been obstruction near the cardia to the passage of the œsophageal bougie, and it must, therefore, have been due to œsophageal spasm of nervous origin, probably connected with the condition of hydrocephalus. In my case (B. S.) the reported absence of free hydrochloric acid from the gastric contents after test meals may possibly be accounted for as of nervous origin, and connected with the hydrocephalus. The condition of "achylia gastrica," though certainly usually associated with organic disease of the stomach, may probably sometimes develop, as writers on the subject have pointed out,[3] from nervous disturbance.

The terminal convulsive seizure in my case, as in others, was probably due to sudden increase of intraventricular pressure acting through pressure on the floor of the fourth ventricle.

In regard to *treatment*, the increase in the morbid symptoms or relapses which have sometimes been observed to follow muscular over-exertion or other kinds of over-fatigue, or even small doses of alcohol, furnishes us with some useful hints for caution, especially in regard to improving cases. There cannot be a doubt that great improvement and even apparent recovery from the symptoms of hydrocephalus in adults occasionally takes place, with or without any special treatment beyond rest in bed, &c. In the present case the improvement was at one time so great that the question of the patient being able to leave the hospital was beginning to be considered. Joslin[1] is not convinced of the usefulness of lumbar puncture in hydrocephalus (at least in his cases following meningitis), but Quincke's results seem to indicate that it may sometimes be of real use, apart from diagnostic purposes, by the temporary relief of pressure.[2] Mercury, iodide of potassium, and possibly salicylates and antipyrin, as well as counter-irritation, are worth a trial, and mercurial treatment epecially may be of service. The improvement sometimes following treatment by calomel, mercurial inunction, and iodide of potassium might in these cases, as in various other brain cases, occasionally lead to an erroneous diagnosis of syphilis.[3]

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[1] Fagge and Pye-Smith's "Medicine," 1901, vol. i., p. 882, Case 4.

[2] *Berliner klin. Woch.*, September 19, 1898.

[3] See Max Einhorn, "Diseases of the Stomach," Second Edition, 1898, p. 328.

Following are some conclusions on the subject of hydrocephalus which I believe are justified :—

(1) That the various kinds of hydrocephalus and effusions into the ventricles of the brain may be fitly compared to the various kinds of effusions into the pleura and the peritoneum.

(2) That the cases of so-called idiopathic or simple internal hydrocephalus are probably nearly all due to more or less localised serous meningeal or ependymal inflammation and are strictly analogous to cases of serous effusion into the pleura or peritoneum, resulting from localised non-suppurative pleuritis or peritonitis. It is of course probable that there are several different microbic or toxic agents.

(3) That the reason why chronic inflammatory thickening of the membrane stretching from the cerebellum to the medulla and forming part of the roof of the fourth ventricle

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[1] *Loc. cit.*

[2] Lumbar puncture for the relief of intraventricular pressure is probably of greatest service in the blood-stained serous effusions resulting from traumatism.

[3] Hydrocephalus in infants in a few cases has been undoubtedly connected with and caused by congenital syphilis. This has been insisted on especially by French writers, and improvement and even cure have been observed under antisyphilitic treatment. See Marfan "L'hydrocéphalie des nourrissons," *La Semaine Médicale*, Paris, 1898, p. 193.

has so often been found present in fatal cases of chronic hydrocephalus, is not necessarily merely that the foramen of Magendie and the neighbouring foramina have been closed by inflammation (as they very often must be in similar cases), but that this portion of the roof of the fourth ventricle is one of the sites of election for the localised inflammation which leads to hydrocephalus.

(4) That the theory of a purely angioneurotic effusion to account for some cases of acute internal hydrocephalus has as yet not sufficient evidence to support it, though doubtless the amount of irritation required to produce the same pressure of effusion varies much in different individuals; it varies doubtless according to conditions (temporary or persistent, congenital or acquired) of the blood-vessels and lymphatics which influence the local circulation; doubtless also temporary circumstances, such as sudden change from the upright to the recumbent position and *vice versâ*, menta or physical exertion, undue exposure to cold or heat, the ingestion of alcohol or other stimulants, and reflex effects on the local circulation from other parts of the body, may influence the tendency to effusion in the ventricles.

(5) That many of the cases of apparently acute hydrocephalus in adults and older children are really exacerbations of a chronic condition, sometimes doubtless dating from early childhood or birth, as evidenced by the history of previous cerebral symptoms, by the relatively large size of the head, or by the *post-mortem* evidence of association with a condition of hydromyelia or syringomyelia, or, as in the present case, by excessive weight of the brain.

Reviews.

Leçons sur les Maladies du Système Nerveux. Par F. Raymond, Membre de l'Académie de Médecine, Professeur des Maladies Nerveuses à la Faculté de Médecine de Paris, Medecin de la Salpêtrière. Quatrième Serie, 1897-98. Cinquième Serie, 1898-99.

The publication of large collections of clinical lectures such as these, delivered from week to week by Professor Raymond at the Salpêtrière clinique, is apparently a tradition peculiar to that great school of clinical neurology since the time of Charcot. Whether such publications, unabridged, are of unmixed benefit is another question. Certainly an interesting series of lectures is the result, but a want of continuity is inevitable and moreover the teacher must perforce repeat the same elementary facts again and again in different connections in order to make each clinical lesson complete in itself.

The individual lectures of the two series, however, are well worthy of perusal, though many are evidently addressed to an audience of comparative beginners in neurological study. Each lecture is a model of clearness in exposition and illustrates the differential diagnosis, the prognosis and the treatment of various diseases of the nervous system.

Amongst the lectures in the fourth series, that on muscular atrophies is of special interest. Professor Raymond maintains that no hard and fast line of demarcation can be drawn between atrophies of myopathic and those of myelopathic origin. As an intermediate class between the two types he instances the peroneal type, associated in France with the names of Charcot and Marie and in England with that of Tooth. English readers may have a little difficulty, however, in recognising Dr. Tooth under the designation of "le medecin anglais Todd." This, the peroneal type of muscular atrophy, resembles the myopathic types in its occurrence in families and in its onset in young people. In another lecture the occasional clinical resemblance between syringomyelia and tabes is brought out, especially in cases where the gliomatosis affects the posterior columns to a preponderating degree. The two diseases may also coexist independently in the cord. A particularly interesting chapter is that on the "phantom" limbs so frequently complained of after amputations. Although many of the sensations referred by the patient to the missing limb are possibly due to irritation of nerve fibres in the scar, yet some are probably central in origin, as in cases where only the most distal segment of the limb seems to be felt, the intermediate part having vanished. Myoclonus and all its varieties are regarded as functional in origin, forming an evidence of a hysterical constitution, hereditary or acquired.

In the fifth series of lectures, a considerable space is devoted to the study of the various forms of localised epilepsy. The most interesting of these is the lecture on the "psychic equivalents" of epilepsy, of which numerous examples are given. Thus in one patient, the attacks of unconsciousness were associated with movements of deglutition, in another patient there were vertigo and hiccough before the unconsciousness and a feeling of amazement afterwards. Another patient had an aura of ravenous hunger. One patient, a woman, had an aura consisting of genital sensations, curiously complete in their sequence. Another female patient had as an aura a feeling of indescribable happiness, so intense that she 'would like to die in it,' her normal mental condition being one of depression and ennui. On the other hand one woman had the converse aura of intense causeless misery, whilst another girl had a feeling of vague fear as if something were about to happen to her. In one case the aura of fear was more circumstantial, the patient seemed to be threatened by a man who had formerly been her lover and the father of her child :—no analogous incident having ever actually occurred in the patient's real life Another girl had an aura in which she felt stupified and during which familiar objects seemed as if they looked strange to her. One man before his attack of epilepsy used to call out in tones of pity to his fellows :—'How pale you are. You are going to fall.' whereas it was himself who turned pale and fell. A still more curious alteration in the sense of personality was that in a woman of thirty who seemed to herself to be someone else whom she herself strove to reach, to try and ward off some impending accident. Another variety of aura is the agonising yet vague effort to remember some word or to find some object. The patient seems to hear a particular word pronounced, and it sounds mysteriously incomprehensible; during the effort to understand this word, the fit occurs. Another case was that of a young man of education who had an obsession consisting in the idea of infinity or eternity, which inspired him with horror. If talked to on this subject on such occasions, an epileptic fit was at once induced. The field traversed in the above observations is one which has hitherto been touched by remarkably few writers on nervous disease, if we except Dr. Hughlings Jackson, of whose observations (dating back to 1879) Professor Raymond seems to be unaware.

There is an interesting description of tuberculous meningitis "*en plaques*." This form, unlike the commoner diffuse basal meningitis of children, chiefly attacks adults, though not exclusively so, and generally the patients are already the subjects of chronic pulmonary tuberculosis. The small extent of the lesions and their habitual localisation in the cortex cause the disease to have quite a special symptomatology. Thus the violent headaches, the vomiting, delirium, ocular palsies, mental torpor, tâche cerebrale, retracted abdomen, slow pulse, &c., which are so characteristic of the common diffuse basal meningitis, are absent in the variety "en plaques." According to the situation of the tuberculous "plaque," the symptoms may be those of aphasia, of incomplete monoplegia, sudden in onset, or of localised convulsions. In exceptional cases, choreiform movements have been observed.

In discussing three cases of sclerodermia, each of them associated with facial hemiatrophy, the author supports the view which teaches that this latter affection is to be ascribed to a neuritis of the trigeminal nerve. Its occasional association with trigeminal neuralgia favours such a view, as also do the pathological reports of cases by Mendel, Frémy and others. The not infrequent association of hemiatrophy of the tongue, which would point strongly in the same direction, is, curiously enough, not alluded to in the discussion.. The absence of anæsthesia or hyperæsthesia, however, shows that the neuritis differs from ordinary neuritis. A toxic origin is not impossible.

The last lecture of the series is devoted to an account of an interesting example of pure word-deafness of hysterical origin.

Enough has been said to show that these lectures are of considerable interest and well worthy of perusal.

PURVES STEWART.

Lehrbuch der Nervenkrankheiten. von Prof. DR. H. OPPENHEIM. 3rd Edition. (Berlin, 1902.)

EIGHT years have passed since the appearance of the first edition of this book, and the time has sufficed to gain for it a world-wide reputation which is scarcely rivalled, and certainly not surpassed, by any neurological text-book in any language. A careful study of the third and most recent edition will convince the student that this fame is fully justified and that the author has striven and successfully striven, not only to bring the volume up to date by the addition of much fresh matter but also to revise and improve the less satisfactory parts of the older work. With these results attained we are now presented with a book of 1,204 pages and with 369 illustrations a respective addition of 230 and 80 to the corresponding figures in the second edition. Besides the greater wealth of illustrations many of the older pictures have with great advantage been more clearly reproduced. Whilst it is impossible to criticise in detail a text-book in which as much importance is given to the views of others as to those of the distinguished author, the absence of any previous notice of the work in BRAIN justifies the selection of a few items for special notice.

Like most German books of the kind this large volume is divided into a "General" and a "Special" part.

The former is comparatively short and consists of some 90 pages devoted to a description of the methods of examining clinically the nervous system with special reference to the significance and relative importance of the various symptoms and signs which are thus evoked in health and disease. There is little here to attract special interest, but it is noticeable that Oppenheim still holds, in spite of Ziehen, Babinski and others, that the absence of the Achilles jerk is not of pathological moment. On the other hand he has made considerable additions to his remarks on the plantar reflex, and not only recognises but fully confirms from his own experience the importance of the so-called Babinski phenomenon.

The chapter on spinal localisation is not as complete as our present knowledge allows, and the deficiency is especially marked in reference to the innervation of muscles and sensory areas by the spinal roots.

The mechanical functions of the various muscles of the body are described with praiseworthy detail and illustrated by means of numerous photographs showing the results of localised palsies and atrophies.

Turning to the voluminous "special" part of the book, which comprises about 1,100 pages, we find many important additions and alterations.

The article on tabes is more profusely illustrated than in th second edition, and reference is made to most of the recent work on the pathogenesis of the disease without advocating strongly any of the different theories as to its conception.

The additions to the clinical and pathological sides of "combined degeneration of the cord" have mostly been culled from the work of English writers to whom suitable acknowledgment is cordially granted.

The chapter on acute anterior poliomyelitis is a lengthy one, especially that part which deals with the differential diagnosis and treatment. A summary of the most recent bacteriological work on this disease is given and a separate article is devoted to the adult form of the same morbid process.

The rare disease which has been called subacute or chronic anterior poliomyelitis and which occurs chiefly in people past the prime of life, is described in full, and the pathological condition found in a case which came to autopsy is reproduced in illustration. Oppenheim regards the process as probably of vascular origin.

The progressive muscular atrophies are divided into two classes, those of spinal and those of muscular origin.

The former includes the ordinary progressive muscular atrophy of the adult and the infantile form first described by Werdnig and Hoffmann. The myopathic class comprises all the varieties of the progressive muscular dystrophies which Oppenheim agrees with Erb in grouping together as belonging to the same clinical and pathological entity.

The clinical varieties are (1) *Juvenile*, developing in youth and middle age and beginning in the shoulder and upper arm. (2) *Pseudohypertrophic*, in which the enlargement of muscles first affects the lower extremities in early childhood. (3) *Infantile*, distinguished by weakness of the orbiculares palpebrarum et oris, generally of congenital origin, and (4) the *Hereditary Form*, where weakness and atrophy of the back and leg muscles appears about the eighth year or later.

Congenital myotonia is fully described and much has been added to his former description from the author's own experience. The view that the disease is due to abnormal development and not to auto-intoxication is strongly supported.

In discussing the etiology of disseminated sclerosis Oppenheim states that it is almost unknown for the onset to occur after 45 or before 14 years of age. He refers, however, to the interesting observation of Eichhorst, who claims to have found anatomical evidence of sclerosis in an immature child whose mother was affected with the disease.

He agrees with English writers in attributing some importance to the occurrence of specific fevers, such as enteric and influenza, in the previous history of the cases.

A most interesting page or two is devoted to the description of atypical forms of insular sclerosis, those numerous cases which do not present the features of Charcot's clinical picture. He says "the disease may resemble spastic spinal paralysis not only in its initial stage but throughout its whole course, more often a combination of spastic paralysis with optic atrophy is observed. . . In late years I have observed a disease in young adults which I was inclined to consider an acute inflammatory affection of the upper cervical and lower bulbar region inasmuch as there appeared an acute ataxy of the upper extremities with bulbar symptoms, a hemiparesis alternans or cruciata, with corresponding alternating extension of sensory disturbance in the face and contralateral side of the body.

"Many of these symptoms quickly disappeared, but the subsequent course of the cases verified the conviction that they were examples of multiple sclerosis."

Two very instructive cases are then cited in which an acute disseminated myelitis followed an attack of typhoid fever; some of the symptoms cleared up but the remainder were followed, after a quiescent period of some years, by the onset of typical signs of disseminated sclerosis of the cerebro-spinal nervous system. The author's advice as regards the treatment of this disease may be summed up in a sentence; promote rest and avoid electricity.

A very graphic description is given of polymyositis, a disease to which little attention has been devoted in this country and which, from the familiarity displayed by German authors with its clinical picture, would appear to be much more common on the continent. In this connection it is interesting to learn that the disease is sometimes called pseudo-trichinosis.

After dealing with the diseases of the peripheral nerves in a most complete and lucid manner the author introduces the chapters on diseases of the brain by an article on the anatomy and physiology of that part of the nervous system. A description of the general symptoms of cerebral disease also precedes the consideration of the individual morbid processes.

Under "the neuroses" the articles on hysteria, neurasthenia and epilepsy are particularly worthy of careful study, and the advice given for the prophylactic and remedial treatment of these conditions contains much that is helpful and suggestive.

Here as elsewhere in the volume Professor Oppenheim introduces much interesting matter from his own large experience, and this is done in such a way as to render the book far more pleasantly readable than is the case with the majority of textbooks. One may add that the names of writers are throughout given in connection with the subjects of their writings, and the addition of a full bibliography at the end would have made the book a most valuable work of reference.

E. FARQUHAR BUZZARD.

Psychology: Normal and Morbid. By CHARLES A. MERCIER, M.B., M.R.C.P., F.R.C.S. (Swan Sonnenschein & Co., 1901.)

IN this book of over 500 pages the author has set himself the difficult task of endeavouring to bring psychology and logic within easy range of each other, and there is no doubt that much earnest thought and discrimination have been brought to bear upon the various problems. Dr. Mercier shows evidence throughout that he has been an enthusiastic student of logic as well as psychology, and to those readers who have already acquired some knowledge of psychology and mental perversions this volume will prove interesting and well worthy of careful study.

Perhaps the author scarcely does justice to the works of others in the various departments of the subject matter, and many will deem his pretensions as inclined to egotism and scarcely warranted by the context. He offers as an excuse for the production of the book the absence of any work in which normal psychological processes are dealt with from the point of view and for the purposes of the alienist, and states that of the many excellent works on psychology which are at the service of the student there is none that affords him material help in understanding the nature of those disorders of mind which it is the work of his life to study, and he deplores the great disadvantage to the alienist to be left without guidance in the face of problems of such profound importance.

Dr. Mercier claims to be the first to enter an "untilled field," and we doubt if he is really serious when he states that the disorders of mind have never before been systematically examined, arranged, and correlated with the normal types from which they erringly depart. He claims allowances if the result displays a certain crudity, the excuse offered being that the axe of the pioneer cannot leave such a finished result as the plane and sandpaper of the subsequent investigator.

When we come to study the context we see that these great claims are scarcely justified.

Sensation is too briefly touched upon. Weber's law is given in the context without any acknowledgment, and a general view of sensation without any reference to the special senses is regarded as being as much as is required for the purpose of the alienist.

The greater part of the book is devoted to "Thought" logically considered, and it is claimed that whereas other logicians have dealt with fallacies at great length and have discussed with minute discrimination the exact nature of the error that has been committed when a wrong conclusion has been arrived at, here an endeavour has been made to show how it comes about that an error has been committed, and to make clear what is the bait and temptation which induces a reasoner to stray from the path and to arrive at a wrong conclusion rather than a right one. In reality most of these pages deal with purely controversial matters within the scope of logic. A strong argument is given in favour of the view that of the fallacies commonly enumerated by logicians, a small proportion only are breaches of syllogistic reasoning—the remainder (the material fallacies) being incapable of reduction to violations of the rules of the syllogism.

When the process of formation of a delusion is considered it would appear as if the application of the results of the chapters on logic were rendered futile by the author's views that the process of formation of a delusion should be dealt with as a fault of mediate or immediate inference. "Delusions come into being in precisely the same way as obsessions by the independent and quasi-parasitic formation of nervous connections which may take place during sleep and which are not necessarily attended by any mode of consciousness; and therefore, if we seek the origin of a delusion among processes of thought we are looking in the wrong direction." He regards the formation of a delusion as not strictly a psychological event—rather is the process closely allied to that to which the name of "unconscious cerebration" has been given.

The remaining chapters deal with volition, memory, pleasure and pain, and subject consciousness, and there are brief applications derived from the study of the normal to those of the morbid.

Every student of psychology will welcome this volume, and it will prove a valuable adjunct to the more comprehensive treatises on psychology. The author's views are expressed in his usual lucid and attractive manner, and the interest is maintained.

THEO. B. HYSLOP.

Healing of Nerves. By CHARLES A. BALLANCE and PURVES STEWART. (Macmillan & Co., London, 1901.)

This is a record of experiments and histological investigation, rather than a treatise upon the subject implied in the title.

The object of the research was to ascertain the processes of degeneration and of regeneration in a peripheral nerve after injury, with and without the suturing of the proximal to the distal segment, and to study the changes which occur in nerve-grafts. The work is chiefly histological, and the most recent methods employed in nerve histology have been brought to bear upon its elucidation. The research has required an enormous amount of skill and labour, and the result is most gratifying; the only regret is that it has not been made the basis of a complete work upon this interesting, and, in view of the large number of gunshot wounds at present occupying the attention of medical men, at present very practical subject.

Of the two theories which are maintained to explain the return of function after division of a nerve, the authors' observations clearly support the "peripheral" as opposed to the "central" doctrine. The peripheral theory is that one according to which the new fibres in the distal segment are formed from pre-existing cells in the distal segment itself. Being thus laid down they become attached later on to those of the central segment, thereby restoring the conductivity of the nerve trunk. The authors therefore adhere to and amplify the results already obtained by Tizzoni, Kennedy, Bethe, and others. As regards the changes which characterise regeneration of a divided nerve, the authors' observations show that they "differ according to whether or not the proximal and distal segments have been brought into apposition. Even in the distal segment of a non-united nerve, regeneration of axis-cylinders and of medullary sheaths takes place, although full maturity of the new nerve-fibres is not attained unless the distal segment be joined to the proximal, so that their fibres may become functionally continuous." The earliest signs of regeneration occur at the end of three weeks. At this time may be seen spider-like neuroblasts shooting out young beaded axis-cylinders from their opposite poles. The new axons rapidly increase in length, and at the end of four weeks have grown so as to overlap and anastomose. The new medullary sheath makes its appearance about the fourth week, it too being laid down by a process of secretion along the side of a spindle-shaped neurilemma cell. Neither axis-cylinders nor medullary sheaths attain to full maturity, unless the distal segment is joined to the proximal: some stimulus obviously is needed to permit of their full development.

From these processes of regeneration in a peripheral nerve trunk, whose connection with its trophic centres has been severed, the authors somewhat arbitrarily propose to discard the neurone theory, in so far at least as it applies to the peripheral nervous system. It would clearly be inadvisable to demolish by one stroke a view based upon the careful embryological and histological observations of His, Waldeyer, Golgi, and others—a view, moreover, which explains many hitherto contradictory facts in connection with the anatomy and functions of the nervous system. There are various points also in the authors' work which would lend support to the neurone theory.

Operative surgeons as well as neurologists will find in this work much to repay its perusal. The book is elegantly printed and bound, and the illustrations do much to enhance the reputation of Mr. Lapidge.

WILLIAM ALDREN TURNER.

Recherches Cliniques et Thérapeutics sur L'Epilepsie, Hystérie, et L'Idiotie. Par BOURNEVILLE, avec la collaboration de MM. de Crouzon, DIONIS DU SÉJOUR, IZARD, LAURENS, PAUL BONCOUR, PHILIPPE et OBERTHUR. Vol. XXI. (Paris, 1901.)

This volume contains as usual an account of the work done at the Bicêtre and the Fondation Vallée. At the former institution there were on January 1, 1900, 449 idiot and epileptic children. During the year sixteen died, eighty-six were discharged, and thirty-five were transferred to other institutions, but a number were admitted, so that on December 31 there were in residence 437 children. A number of cases are related showing the improvement made by the system of training employed in both institutions. There had been an outbreak of scarlet fever, measles, chicken-pox, and mumps; two children had had diphtheria and one erysipelas. At the Fondation Vallée there were 199 children at the beginning of the year; of these eight died, twenty-three were discharged, and seventeen were transferred chiefly to the institution at Villejuif. A number were admitted, so that there were 213 residents at the close of the year.

Dr. Bourneville again urges on the authorities the advisability of establishing special classes for backward children, as has been done in England, and gives an account of the work done by these classes in Italy, Holland, and Berlin. It appears that though 1,068 beds are provided for idiot and epileptic children in the four institutions at Paris, a large number are still waiting for admission, and the prefect of the Seine suggests that a number of vacancies would be made by erecting another building, or enlarging the existing institutions; by transferring the children at the Bicêtre as they arrive at adult age to the adult department of the Salpêtriére; by the creation of special classes for backward children; and by sending home some of the cases and paying their parents a franc and a half or two francs per week towards their maintenance. Dr. Bourneville generally approves of these methods for providing vacancies.

The second part of the book contains a number of essays written by Dr. Bourneville and his assistants. One of these is an account of a case of profound idiocy which remarkably improved after being trained for four years. The child was four years old when admitted, was unclean in his habits, violent, and practised masturbation. He could not speak. He was put into the school with the little children, and after being there ten months became cleaner in his habits, was less violent, but could not speak. Six months later he began to pronounce some words, and was still less violent. At the end of another six months his speech was much more intelligible, he was quite clean in his habits, and could dress and undress himself. This amelioration continued, so that when he was taken home by his mother contrary to the advice of Dr. Bourneville, he spoke quite correctly, wrote some letters, and had commenced to read books.

In another essay the author makes a fresh enquiry into the part which consanguinity plays in the etiology of epilepsy, hysteria, and idiocy and imbecility. He finds that from the year 1879 up to December 31, 1900, at the Bicêtre, and from 1890 to December 31, 1900, at the Fondation Vallée, 2,784 cases had passed through his hands. Of these, ninety-one cases had been noted which were said to be due to consanguinity, or 33 per cent. On going further into the history of these cases, it was found that the influence of heredity was very marked. Dr. Bourneville concludes that if cousins of vigorous constitution and with no hereditary taint marry normal children will be born, but if one or both have a bad hereditary history their children will, not as the result of consanguinity but of hereditary taint, be affected with mental or physical degeneration, epilepsy, hysteria, and idiocy.

Another paper goes into the question of the action of alcohol on the production of idiocy and epilepsy. Children suffer from the action of alcohol in various ways: (1) as a consequence of the chronic alcoholism of the father or mother or both parents; (2) as the result of the drunkenness of the father at the moment of coition; (3) during fœtal life, in consequence of the alcoholism of the mother, excited emotions are experienced during pregnancy; and (4) because the same alcoholic excess and the same emotion exists when the child is at the breast and subsequently. Dr Bourneville examines the histories of 2,554 cases, and he finds that 41·1 per cent. of the parents have drunk to excess, and 41·1 per cent. were sober. This shows the dangerous action of excessive imbibition of alcohol.

In another essay the results of the histological examination of hydrocephalus idiocy, of idiocy caused by meningo-encephalitis, of idiocy and epilepsy with atrophic sclerosis of the frontal lobes, of idiocy, epilepsy, hemiplegia as the result of excessive drinking of alcohol by the parents, and of idiocy with cerebral atrophy, pachymeningitis and cyst of the dura mater are given at length. The following paper contains a histological resumé of the cases which have been studied.

Another essay which deserves notice is on the influence of unhealthy occupations on the production of chronic diseases of the nervous system. It is known that the children of workers in white lead, mercury, phosphorus, and copper suffer from idiocy imbecility, and intellectual and moral weakness, and Dr. Bourneville shows this bad influence on the children by means of a table in which the histories of eighty-seven families which worked in these trades have been specially enquired into. It is shown, first, that the eighty-seven families produced 420 children, or an average of five children to each family; secondly, that of these 420 children 220 died; and thirdly, that if to the 220 deceased children the eighty-seven idiots and epileptic children are added, it will be found that 73 per cent. of the children are mortally or gravely affected by the unhealthy occupations of the parents. A number of photographs of patients whose cases are related in the book, and eleven photographs of brains which had been removed and examined, add greatly to the interest of the volume, and show that Dr. Bourneville and his assistants are still hard at work, and making every possible use of their experience at the Bicêtre and Fondation Vallée.

FLETCHER BEACH.

Pathologie und Therapie der Herzneurosen und der functionellen Kreislaufstorungen. von Dr. AUGUST HOFFMANN, in Dusseldorf. (Verlag von J. F. Bergmann 1901.)

In the preface to this book Dr. Hoffmann refers to the increasing interest taken by the medical profession in the functional, as opposed to the organic, diseases of the heart, as an excuse for the appearance of a monograph on the subject. He pays a graceful tribute to Gaskell, Engelman, and others for their share in stimulating this interest from a physiological standpoint.

In introducing his subject the author lays considerable emphasis on the ill-defined boundary which at present exists between organic and functional disturbances of the heart, and points out that amongst the latter must be included all so-called cardiac neuroses, whether they are of nervous or muscular origin.

The book is divided into a "General" and a "Special" part; the former includes a chapter on anatomical considerations, in which the author presupposes a general knowledge of anatomy on the part of the reader, and devotes a good deal of attention to variations in the mobility of the heart and to the effects of changes in the position of the body generally on the relative intra-thoracic geography. Eleven pages are dedicated to a good *résumé* of the most recent physiological work on the automatism of the heart, the influence of the vagus, sympathetic and other nerves, the extra-cardial nerve-centres, and the phenomena of cardiac contraction.

Reference is made to the fact that we have yet to discover a special cardiac centre at a higher level than the medulla oblongata. Methods of examining the heart and vascular system are described in some detail, and the results of such examination in dealing with simple functional disturbances or similar disturbances accompanying organic cardiac diseases are reviewed in the subsequent pages.

Speaking generally, this part of the book brings together a large number of facts, and gives a copious reference to the work and opinions of other observers, without the addition of many new ideas originating with the author himself. The same remark applies to the second or "Special" part, in which are collected and discussed, under suitable heads, all the various conditions wherein cardiac neuroses are liable to occur either primarily or secondarily.

An article of some length is here devoted to cardiac Neurasthenia, and the author attempts to classify the varieties of this complaint in a manner which differs slightly from that adopted by Rosenbach and Lehr. He separates those neurasthenics in whom the subjective symptoms of cardiac trouble predominate, from those in whom the objective signs are most noticeable, but admits that one person may present the characteristics of either class at different times. One cannot help thinking that such a classification is more applicable in theory than in practice, whilst one agrees with the author in regarding the subjects of well-marked objective cardiac irregularities as more needful of careful observation and in greater danger with regard to the supervention of organic lesions.

In discussing the pathogenesis of Adam-Stokes's symptom-complex, Hoffman inclines to the view that the marked slowing of the pulse is due to the failure of the normal contraction wave from one part of the heart to another, and exemplifies a case of his own in which, by transmitted light, he was able to observe minor auricular contractions unaccompanied by ventricular systole or arterial pulsation. This failure of conductivity may, in his opinion, be the result either of local abnormalities in the cardiac ganglion-cells or muscles, or be secondary to some functional influence on the part of the vagus nerve, and the theory is advanced for the purpose of covering not only those cases of this disease in which organic lesions are present, but those also in which no demonstrable cause can be found after death.

The descriptions of many other so-called neuroses, such as Basedow's disease, Raynaud's disease, Erythromelalgia, acroparæsthesia, and the like, are by no means exhaustive, and the student can only use them as a basis for wider reading. This is facilitated by the presence of a useful bibliography of each subject. A name-index and a contents-index complete a volume which may be regarded as a careful compilation of the facts and theories concerning cardiac and vascular neuroses, without any attempting to throw new light on their obscurity.

E. Farquhar Buzzard.

PROCEEDINGS OF THE NEUROLOGICAL SOCIETY OF LONDON.

At a Pathological Meeting held at 11, Chandos Street, on Thursday, March 13th, at 8.30 p.m., the following Communications were made:—

Dr. SINGER.—*Remarks upon the pathology of so-called acute myelitis.*

The morbid anatomy of two cases terminating fatally within eight weeks of the onset of symptoms. Presence of thrombosis due to syphilitic arteritis in the vessels of the affected area of the spinal cord in a man aged 53. Overgrowth of interstitial tissue around the vessels in the region of the lesion in a child the subject of congenital syphilis. Complete absence of any evidence of acute inflammatory change at the site of the lesions. Clinical evidence in support of the thrombotic origin of many cases of so-called acute myelitis.

Dr. COLLIER.—*The degenerations resulting from the local lesions in Dr. Singer's cases examined by the Marchi method.*

Descending Degenerations.—The descending fibres of the posterior columns occupying successively the cornu-commisural region, the comma tract, the septomarginal tract, the oval area of Flechsig, and the peripheral zone and triangular area of Gombault, and Philippe, belong to one and the same system; this conclusion agrees entirely with those of Nageotte and Ettlinger, Purves Stewart and others.

The absence of evidence that descending collaterals of the posterior roots occupy a position corresponding to that of the comma tract.

Ascending Degeneration.—The ascending fibres of the dorsal longitudinal bundle. The ascending spino-thalamic and spino-tectal fibres. The sacro-cerebellar tract of Rothmann. The so-called crossed ascending sensory path.

Dr. F. PARKES WEBER.—*The brain from a case of chronic internal hydrocephalus in an adult.*

Dr. J. WAKELIN BARRATT.—*Sections illustrating fibrin formation in hæmorrhagic internal pachymeningitis.*

Writers of "Original Articles and Clinical Cases" are supplied free of charge with 50 copies reprinted in the form in which the paper stands in the pages of "Brain." If reprints are required in pamphlet form, with wrapper, title page, &c., and re-numbered pages, they must be ordered, at the expense of the writers, from Messrs. BALE, SONS & DANIELSSON, Ltd., 83-89, Great Titchfield Street, London, W.

BRAIN.

PART II., 1902.

Original Articles and Clinical Cases.

ON PACHYMENINGITIS HÆMORRHAGICA INTERNA.

BY J. O. WAKELIN BARRATT, M.D.LOND., F.R.C.S.ENG.
Pathologist to the West Riding Asylum, Wakefield.

THE present research has been undertaken with the object of attempting to elucidate the mode of production of hæmorrhagic internal pachymeningitis. A three-fold investigation has been pursued: the histological appearance of hæmorrhagic internal pachymeningitis has been studied, and the observations of previous workers repeated; a bacteriological examination of subdural false membranes has been made; and implantation of portions of these membranes into the subdural space of animals has been practised. While studying the histological characters of subdural membranes, intravascular thrombi consisting of fibrin fibrils were repeatedly met with, the existence of which has not, so far as I am aware, been previously recorded.

The results of this investigation will be described in three sections, dealing respectively with (1) intravascular thrombosis; (2) the bacteriological examination of the membranes; and (3) the effect of subdural implantation. As a preliminary it is, however, necessary to give a brief account of the naked eye and histological appearances of hæmorrhagic internal pachymeningitis, and to present as accurately as possible the essential features of its development according to the various observers who of recent years have made researches upon this condition, the statements made being verified whenever possible by my own observations.

The Structure of the Membrane.

The fully formed membrane of hæmorrhagic internal pachymeningitis consists of a very delicate, more or less grey or brownish-grey œdematous layer, lying upon, and adherent to, the inner surface of the dura mater, and exhibiting large thin-walled dilated vessels together with extravasations of blood of varying size. On the free surface of the membrane is generally found a very thin layer of fibrin.

According to the extent to which these different characters are developed subdural membranes vary much in aspect. Sometimes there is little or no injection or extravasation and the membrane is of a greyish aspect. Sometimes a number of fine dilated vessels just visible to the naked eye, arranged in small foci ranging in diameter from one millimetre to several centimetres or more, and not unfrequently partially coalescing, are observed, together with few or numerous extravasations of blood of varying size. In yet other cases the striking feature is hæmorrhage, which may take place to such a degree that it is impossible to recognise in the subdural space, either on inspection or by microscopical examination, anything but blood-clot. The first and last of these constitute two extreme types of subdural membrane; the usual form is more or less mixed in character. The extravasations of blood when of large size produce depressions on the surface of the brain, and when of old standing, become converted into a stratified brownish-red soft friable mass, perhaps containing collections of semi-fluid material, the whole being surrounded by a fibrous sheath. To this latter condition the terms arachnoid cyst, hæmatoma of the dura mater, and subdural blood cyst have been applied.[1]

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[1] *Cf.*, for further description, "Report on a Subdural Blood Cyst," BRAIN, Vol. xxiii., pp. 530-541, 1900.

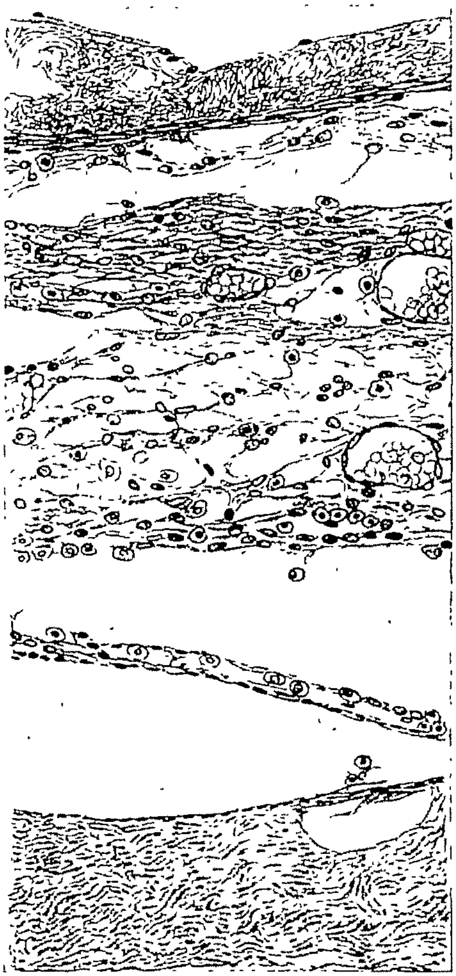

FIG. 1.

The false membrane varies in thickness from a fraction of a millimetre up to two or three millimetres or more.

The points to be noted in searching for subdural membranes in their earliest stages are: dulness of the inner surface of the dura mater, replacing its usual shining silvery character; congestion of the dura mater, chiefly on its inner surface; and the presence of hæmorrhages. When the dulled area of the dura mater is scraped the greyish pellicle by which it is covered is detached, and its features are readily observed.

The membrane is usually adherent to the inner surface of the dura mater. Occasionally, though rarely, it is adherent to the pia-arachnoid, and sometimes the subdural space is obliterated by adhesions to both dura mater and pia-arachnoid. The preponderant tendency to adhesion to the dura mater is in part due to the circumstance that this membrane presents a ridged inner surface not covered by a distinct layer of endothelial cells, while the latter membrane is quite smooth and has an abundance of flattened cells on its free surface; in part also to the fact that the development of the false membrane takes place from the inner surface of the dura.

Old standing membranes are much firmer than recent ones, and assume a brownish-red or rusty aspect, owing to the presence of pigment in many of the cells of the subdural formation.

It is, however, to the microscopical characters of hæmorrhagic pachymeningitis that we turn in forming an opinion as to the nature of the pathological process at work and the mode of development of the false membrane.

In hæmorrhagic pachymeningitis of some standing, a transverse section shows the existence upon the inner surface of the dura mater, of a layer composed of delicate wavy connective tissue fibres (fig. 1), which interlace to form a loose network, the spaces of which usually contain a large amount of fluid. In this connective-tissue framework are found a large number of cells, some of which resemble the endothelial cells seen in small numbers on the inner surface of the dura, and in much larger numbers on the outer surface of the pia-arachnoid, while others are free or but loosely attached. The latter cells possess sometimes but little protoplasm; sometimes they exhibit large cell bodies and form striking objects in the field of the microscope. Some of these free cells contain brownish-red pigment, obviously derived from red blood-cells, others again are free from pigment; the former are macrophages, the latter resemble the former in every respect save that of containing blood pigment. The amount of pigment present in the cell-protoplasm varies from an extremely small quantity to a collection so abundant as to fill the whole of the cell body and obscure the outline of the nucleus. In addition to these cells the connective tissue framework contains very numerous thin-walled dilated blood-vessels, the presence of which is a distinctive feature of the membrane. The walls of these vessels are made up of a layer of endothelial cells, no adventitia or muscular coat being seen. Here and there extravasations of blood are met with. Not unfrequently the red cells are broken up into granular débris, having a yellowish tint. On the surface of the membrane is a deposit of fibrin, sometimes in the form of fine fibrils (figs. 2 and 3), sometimes in the form of a granular amorphous material in which no structures are seen except an occasional nucleus, or rarely a single blood-capillary; both the fibrils and the granular material, especially the latter, take up dyes [including not infrequently fibrin stains] badly. As a rule this deposit is found only on the surface, but it is also, though rarely, met with in the meshes of the connective tissue frame-work. Intra-vascular development of fibrils also occurs and forms a striking feature in most sections of recent membranes. Its consideration will be taken at some length in the next section.

The dura also exhibits changes chiefly but not exclusively in its inner layer. The nuclei at its inner surface lying upon the internal elastic lamina are increased in number and size, as are also, but in less degree, the nuclei below this lamina. The blood-vessels of the inner layer of the

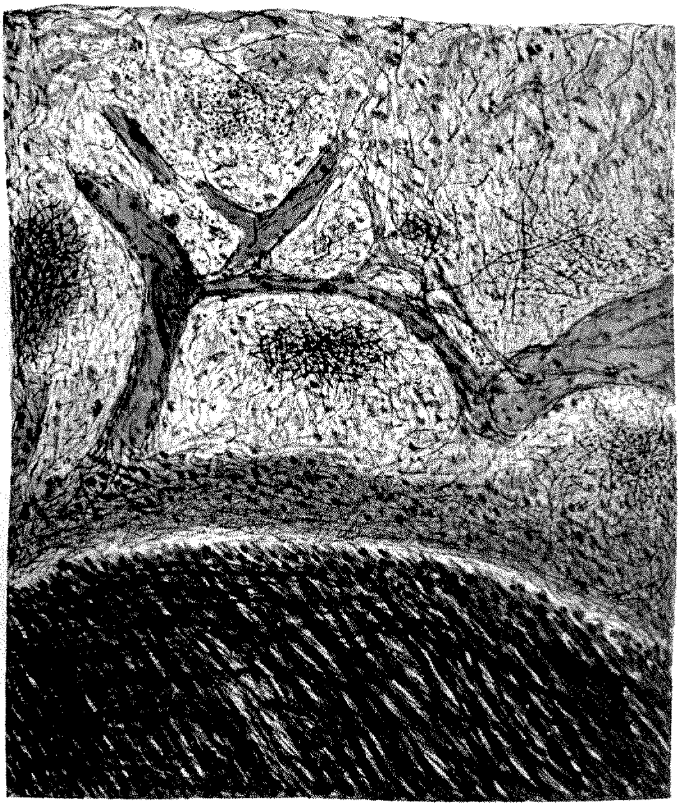

FIG. 2.

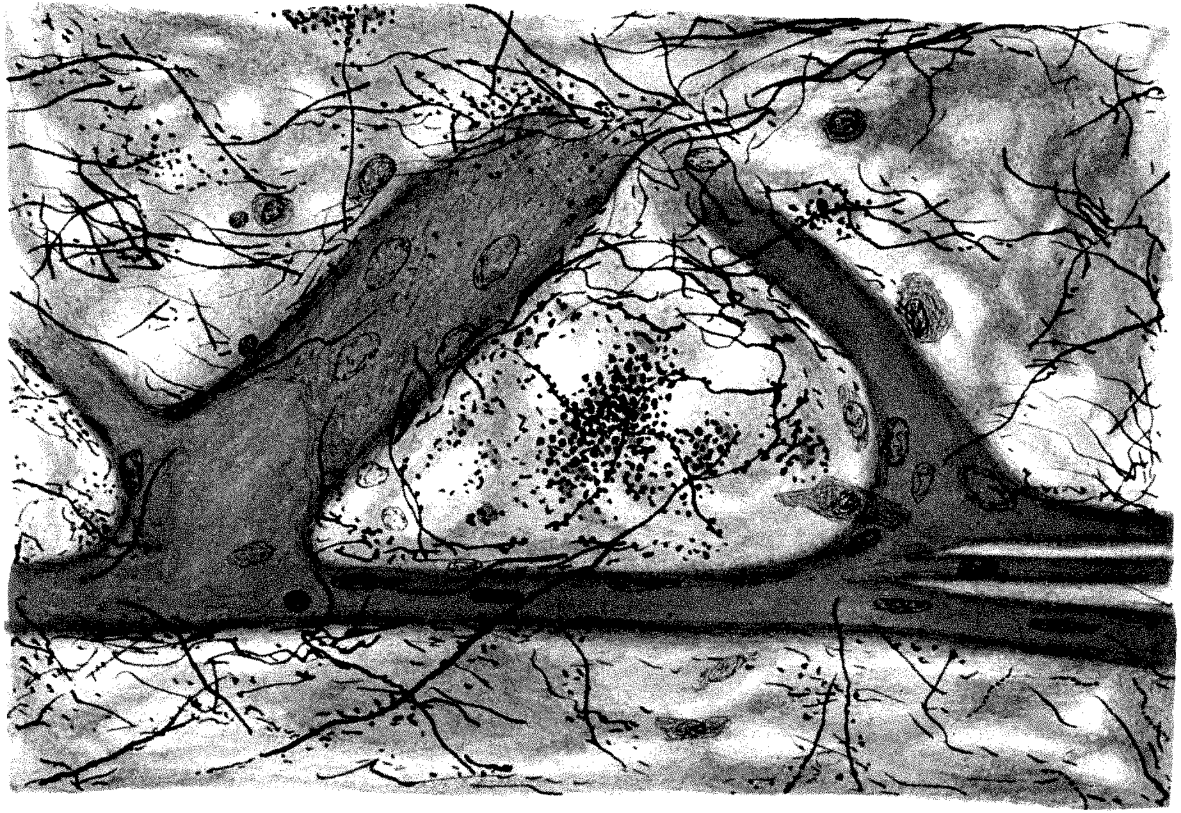

Fig. 3.

dura, which are continuous with those of the membrane, are dilated and increased in number. A similar dilatation much less in degree, is met with at the outer surface of the dura mater.

Much discussion has taken place as to the nature of hæmorrhagic pachymeningitis, and various views have been enunciated by different observers. These, though varying in points of detail, fall into two main groups, recalling the two extreme types referred to above; according to some investigators the process has its origin in hæmorrhage into the subdural space, and all the subsequent events leading up to the development of a fully formed membrane are secondary to this; by other observers, including Virchow, it is regarded as inflammatory in its nature, and hæmorrhage, though distinctive, is looked upon as only one of the events which make up the morbid process.[1] The settlement of this point turns upon a consideration of the initial events which lead up to membrane formation. These latter furnish also criteria by which to determine the nature of any subdural process produced experimentally.

The earliest changes[2] recognisable in hæmorrhagic pachymeningitis are swelling and proliferation of the endothelial cells on the inner surface of the dura mater, dilatation of the capillaries of the inner layer of this membrane, and exudation of fibrin forming a layer upon the free surface of the dura. Then free cells possessing a variable amount of cell-protoplasm together with fibroblasts and new capillaries appear in the exudation, which ultimately is replaced by fibrous tissue. Hæmorrhage though not invariable is common, usually giving the membrane its characteristic aspect, but it is not a necessary[1] prelude to the formation of a subdural membrane.[2]

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[1] Hæmatoma duræ matris. *Verhandl. d. phys. med. Gesellsch zu Würzburg*, 1856, Bd. vii. For a discussion of this subject reference may be made to Ford Robertson's article in his "Text-book of Pathology in Relation to Mental Diseases," pp. 80-116, in which copious references to the literature of the subject up to 1896 are given.

[2] Compare Melnikow-Raswedenkow, "Histologische Untersuchungen über den normalen Bau der Dura Mater und über Pachymeningitis interna." *Ziegler's Beiträge zur patholog. Anatomie*, Bd. xxviii., pp. 217-254. Also Laurent, "Zur Histogenese der Pachymeningitis hæmorrhagica interna." *Inaug. Dissert.*, Düsseldorf, 1898. Also "Jores, Ueber die Beziehungen primärer subduraler Blutungen zur Pachymeningitis hæmorrhagica." *Verhandl. der deutschen patholog. Gesellsch.* I. Tagung, Berlin, 1899, pp. 49-62.

In fig. 1 the structure of a false membrane is shown in transverse section. This figure is stained by hæmatoxylin and picro-fuchsin. Protoplasmic staining is difficult, probably because of the œdematous character of the membranes injuriously influencing the cell protoplasm prior to fixation. Occasionally mast-cells are recognisable, the granules of which are being discharged. I have not obtained satisfactory plasma-cell staining.

In figs. 2 and 3 is shown a section of a recent fibrinous exudate. Numerous vessels of new formation are seen, which are empty, and though large are not distended to a marked degree. Note that no extravasation of blood is seen, and no cells are seen containing hæmatoidin.

Intravascular Thrombosis.

When a section of a recent subdural membrane is stained by hæmatoxylin there is found in a certain number of blood-vessels, which are usually distended with blood, a mass of fibrils, the presence of which appears to have been strangely overlooked by previous observers. As soon as the appearance of these has once been observed they are readily recognised even when imperfectly stained (fig. 4). They are best coloured by Weigert's fibrin stain, by means of which they can be sharply differentiated (fig. 5). The number of these fibrils is very variable. Sometimes most of the blood-vessels are free from them, and only here and there are a few encountered; in other cases they are found in the majority of the blood-vessels examined. When present they may lie among the red cells, occupying but a small portion of the lumen of the vessel, as in fig. 5, or

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[1] According to Melnikow-Raswedenkow pachymeningitis interna generally develops without preceding hæmorrhage [*loc. cit.*, p. 247]. Ziegler discussing Jores' paper (*loc. cit.*) "Hält darin fest, dass die Membranbildung der Pachymeningitis mit Fibrinabscheidung beginnen kann. . . . Ob der Process immer mit Fibrinabscheidung beginnt, lässt sich nicht entscheiden."

[2] In Table I. it will be seen that in all but one out of the twenty-four cases examined wasting of the brain mantle was present, and that with one exception this was accompanied by opacity and thickening of the membranes. The degree in which these two characters were present is also indicated in this Table.

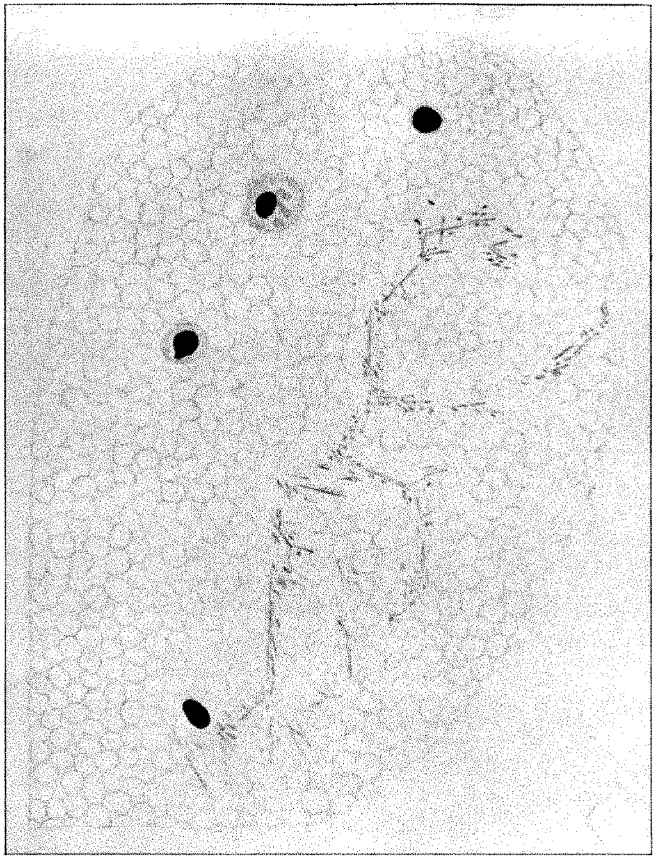

Fig. 4.

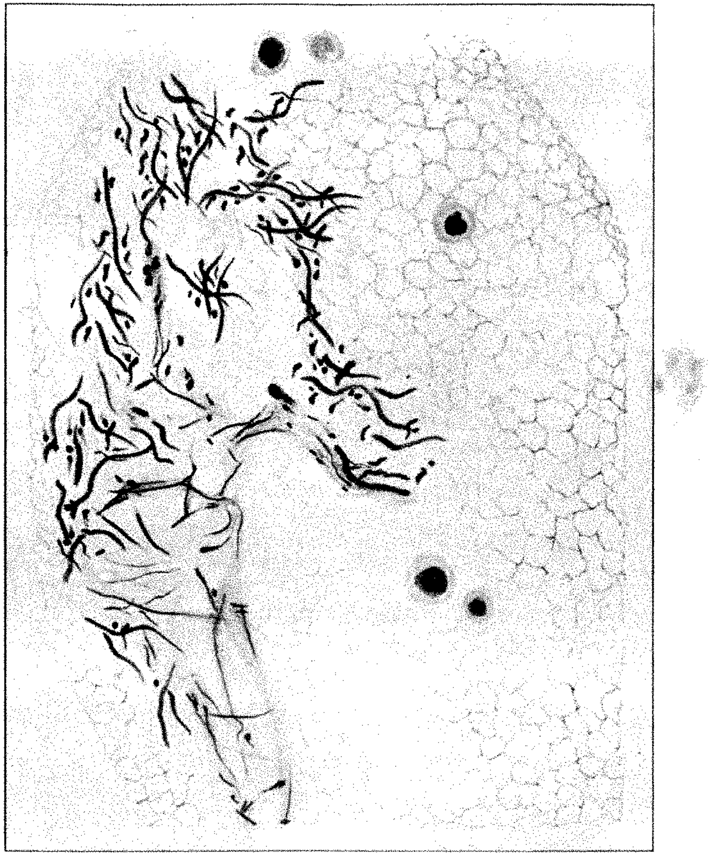

Fig. 5.

they may completely fill it. They are found in small vessels as well as in those of larger calibre. The individual fibrils vary in size from $\cdot 5\mu$ to 2μ, and cross each other in different directions; when numerous, and especially in the smaller vessels, they tend to be arranged in the axis of the vessel. The larger fibres stain more readily than the smaller. The fibres remain separate from one another. They do not branch or anastomose. Sometimes both large and small fibrils show a coarsely or finely granular character, but otherwise the fibrils are quite structureless. Not unfrequently they are surrounded by red blood cells, but they may occur in portions of blood-vessels which are quite free from red blood cells or contain such cells only at some distance from the fibril mass. Red blood cells are sometimes contained in the meshes of the fibrils, more often they are wanting in this situation.

With logwood and eosin, methylene and polychrome blue, thionin, and orcein, these fibrils stain imperfectly. They are, however, generally tinted sufficiently to enable their presence to be recognised, though details of their arrangement are not apparent. As it is important to be able to recognise their existence in the absence of special staining, fig. 4 is given. In fig. 5 are seen fibrils deeply stained by Weigert's method; this figure is similar to the former, with which it should be compared. The fibrils in fig. 4 are just recognisable, and it can be seen that their direction is mostly transverse or oblique, only a few running parallel to the plane of section. After a short study of these two sections it is not difficult to interpret the appearance of the fibrils in question when imperfectly stained.

In appearance and staining reaction these fibrils are identical with the fibrin threads found in fibrinous inflammations. It is obvious that they form in the vessels during life, for whatever method of hardening is used (alcohol, bichromate of potassium, formol) they are found very irregularly distributed in the vessels of the false membrane, while those of the pia-arachnoid are free from them. Intravascular thrombi of fibrin are met with in various pathological conditions, principally in fibrinous inflammations, *e.g.*, lobar pneumonia, but also though less conspicuously and probably much less frequently in other morbid states, not necessarily hæmorrhagic in character.[1] Putting aside fibrinous inflammations, however, their presence does not appear to be common in affections other than hæmorrhagic pachymeningitis, in which their constancy and abundance is a striking feature.

The intravascular fibrils, as has just been stated, stain readily with a fibrin stain. The fibrils which are deposited on the free surface of a subdural membrane or of the dura mater in the early stages of hæmorrhagic internal pachymeningitis (figs. 2 and 3) also stain with a fibrin stain, but not as a rule so readily as the former. This difference appears, however, to be due to the smaller size of the latter, for the intravascular fibrils stain more deeply the larger they are, the smallest not unfrequently staining with some difficulty. The fine surface fibrils sometimes exhibit the same granularity as the intravascular fibrils. The granular fibrinous deposit on the surface of a membrane or of the dura mater is still more difficult to stain deeply than is the fibrillary formation.

Masses of fibrils appear to be always present in false membranes when recent and progressive, as indicated by the presence of extravasations of blood, while they are absent in old membranes in which the morbid process has ceased. Thus in Table I. it is seen that out of twenty-three subdural formations[2] in which this point was recorded fibrils were seen in seventeen, and could not be found in six. Of the latter two consisted almost entirely of flattened blood-clot, and the remaining were of old standing, being rusty coloured or grey, and free from extravasations of blood. In subdural blood-clot search for the hæmorrhagic pellicle originally present is necessarily difficult and unlikely to be successful. In the vessels of the pia-arachnoid fibrils were rarely observed, even when a subdural pellicle was present. As is well known hæmorrhages occur far less frequently in

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[1] For example, I have met with them in carcinoma, cholecystitis, cerebral tumour, in the ovary near a corpus luteum, &c.

[2] These formed a series, the order of which has been altered for convenience of reference in the Table.

TABLE I.—SHOWING THE CONDITION OF BRAIN, PIA-ARACHNOID AND SUBDURAL MEMBRANE.

No. of Case.	Condition of Brain Mantle.	Opacity and thickening of pia-arachnoid.	Appearance of Subdural Membrane	Fibrin in Membrane [intra- and extra-vascular.]	Bacteria in Sections of Membrane. Loeffler's Method.	Bacteria in Sections of Membrane. Gram's Method.
1	Slight wasting	Present	Thin. Brown pellicle	[No sections cut]	[No sections cut.]	
2	No wasting	Slight	2 to 3 mm. thick. Made up of blood-clot	None found	None	None.
3	Very slight wasting	Slight	Thin. Made up of blood-clot	None found	None	None.
4	Slight wasting	Slight	Thin. Grey, transparent, of old standing	None found	None	None.
5	Wasting	Present	Thin. Grey, of old standing	None found	[See Table ii.]	
6	Wasting	Absent	Very thin. Rusty pellicle	None found	None	None.
7	Marked wasting	Present	½ mm. thick. Rusty, firm, fibroid	None found	[See Table ii.]	
8	Wasting	Slight	1 to 1½ mm. thick. Hæmorrhagic, in places rusty	Uniform filaments	None	None.
9	Marked wasting	Present	3 mm. thick. Hæmorrhagic and œdematous, in places rusty	Fine filaments, uniform and granular	None	None.
10	Slight wasting	Slight	1½ mm. thick. Numerous hæmorrhages and dilated vessels	Well-formed, uniform filaments	None	None.
11	Wasting and compression	Slight	1 mm. thick. A large blood-cyst present	Uniform filaments	None	None.
12	Wasting	Slight	½ mm. thick. Both old and recent; hæmorrhagic	Fine, uniform fibrils	None	None.
13	Wasting	Slight	½ to 1 mm. thick. Hæmorrhagic	Fine, uniform filaments	None	None.
14	Wasting	Slight	2 mm. thick. Numerous hæmorrhages	Septate filaments	Short bacilli	Unstained.
15	Wasting	Slight	Very thin. Made up of blood-clot	Septate filaments	None	None.
16	Marked wasting	Present	Very thin. Hæmorrhagic	Uniform filaments	None	None.
17	Wasting	Present	Very thin. Greyish-red	Uniform filaments	None	None.
18	Wasting	Present	1 mm. thick. Pale grey, hæmorrhagic	Uniform filaments	None	None.
19	Wasting	Present	Very thin. Not hæmorrhagic; recent	Uniform filaments	None	None.
20	Wasting	Slight	1 to 1½ mm. thick. Whitish-grey, numerous hæmorrhages	Fine, uniform filaments	None	None.
21	Wasting	Slight	1 mm. thick. Greyish-red pellicle	Fine, uniform filaments	None	None.
22	Marked wasting	Present	½ mm. thick. Grey, no hæmorrhages	Uniform and granular filaments	[See Table ii.]	
23	Wasting	Present	Thin. Brown, hæmorrhagic	Fine, uniform filaments	None	None.
24	Wasting	Present	1 mm. thick. Pale, hæmorrhagic, in places rusty	Very few filaments	None	None.

the leptomeninges than in the subdural space, but are, nevertheless, occasionally met with.

It has already been mentioned that the fibrin fibrils seen in the blood-vessels are sometimes few in number, forming an open meshwork occupying only a fraction of the lumen of the vessel (figs. 4 and 5), while in other cases the filaments are numerous and form a large plug, which completely fills the vessel, and obviously offers an obstruction to the passage of blood. Bearing in mind the frequency of hæmorrhage in pachymeningitis the enquiry at once presents itself, are these intravascular plugs the cause of vascular rupture.

The frequency and constancy with which they are met with in this affection is as distinctive as is its hæmorrhagic character, so that their existence cannot be considered merely coincidental, or due to separation of fibrin at the time of death. Another feature in hæmorrhagic pachymeningitis, which is as striking and as distinctive as the appearance of extravasation of blood, and is present even when the latter is small in amount, is the occurrence of vascular dilatation. It seems clear that the existence of fibrin plugs in the vessels, by causing obstruction, leads first of all to dilatation, and thus opens the way to subsequent rupture. In this way an explanation is afforded of two of the chief features of subdural membranes. It is impossible to imagine that the process of intravascular clotting is other than the immediate factor leading to dilatation of vessels and extravasation of blood, and it is therefore to this circumstance that both these events must be attributed.

The relation of intravascular thrombosis to the deposit of fibrin on the surface of the dura mater or of the false membrane must now be considered. Both these processes occur together, and are evidently the result of the same cause, producing in the one case a deposit within, and in the other without, the blood-vessels, with the difference that large fibrils are usually produced in the former situation, and very fine fibrils or a granular deposit in the latter.[1] In the membrane, except on the surface, a deposit of fibrin is rarely met with. Perhaps owing to the presence of free cells within the membrane itself, the conditions here are not so favourable for the separation of fibrin as on the surface, and its occurrence is therefore unusual. Occasionally, however, well formed fibrin filaments are met with in the meshes of the fully formed subdural membrane. These, which are only rarely seen, sometimes exactly resemble the fibrinous plugs in the larger vessels, and are apparently due to their escape from the ruptured vessels, but in other cases a true interstitial formation of fibrin fibrils is met with.

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[1] The membrane shown in figs. 2 and 3 contains large fibrils, however, in abundance.

In respect of the origin of the separated fibrin appearing both within and without the blood-vessels in hæmorrhagic pachymeningitis, reference may be made to the observation of Halliburton[1] that nervous tissue contains a nucleo-proteid, which readily causes clotting when introduced into the circulation. The presence of such a body suggests a ready explanation of the separation of fibrin, which forms such a striking feature in subdural membranes. It must, however, be conceded that the demonstration of the presence of this nucleo-proteid in subdural formations has yet to be made.

The view here advanced that the intravascular thrombosis is the cause of the dilatation and subsequent rupture of the newly formed blood-vessels in hæmorrhagic pachymeningitis exhibits this process in a new light, its leading character being the separation of fibrin within or without the vessels, leading in the one case to hæmorrhage from the dural vessels, and in the other to exudation on the surface of the dura. A reconciliation is thus foreshadowed between the conflicting views as to the priority of hæmorrhage, as probably most observers hold, or that of fibrinous exudation, as has recently been advocated by Jores and Melnikow-Raswedenkow. How far the early dilatation of the vessels of the inner layer of the dura mater and the multiplication of nuclei on its inner surface are to be regarded as reparative in nature, and how far these are to be attributed to the direct effect of the conditions favouring separation of fibrin remains yet to be determined. The later events which attend upon exudation of fibrin and hæmorrhage, namely, the appearance of free cells, many of which are filled with blood-pigment, together with fibroblasts and vaso-blasts, are obviously chiefly, if not wholly, reparatory. This point will be again referred to in the last section.

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[1] *Journ. of Physiol.*, 1893, vol. xv., pp. 90-107.

The filaments met with constantly in the blood-vessels, and less frequently and less abundantly in the spaces of the membrane or upon its surface, are here regarded, for the reasons already given, as fibrin filaments. They present at first sight some resemblance to a mycelium, but usually consist of quite uniform fibrils, not exhibiting septa, spores, or gonidia. In two cases, however, out of the fifteen examined (14 and 15, Table I.), some of these filaments were found to present a septate or granular aspect, both large and small filaments being affected[1] (figs. 6 and 7), while there was also a tendency to peripheral staining, giving a hollow character to the filaments. In the first of these cases bacteria were present. The appearance was probably produced subsequently to death, both large and small filaments being involved. Bearing in mind the failure to obtain cultures of fungi from the membranes, recorded in the next section, and the identity in morphological and staining characters of the filaments in all the remaining cases to fibrin fibrils, there seems to be little doubt that these filaments are not fungoid in character, but are merely fibrin filaments altered in character by events occurring *post mortem*. In the third stage of pneumonia the fibrin filaments still remaining may present a beaded character, but I have not met with a distinctly septate character so well marked as in figs. 6 and 7.

While separation of fibrin plays an important part in the initial stage of subdural membrane formation, it must be pointed out that this process does not closely resemble that occuring in acute fibrous inflammations, such as pneumonia. The latter is the result of the action of an intense irritant leading to the appearance of an abundant

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[1] In fig. 3 also some of the finest filaments are beaded.

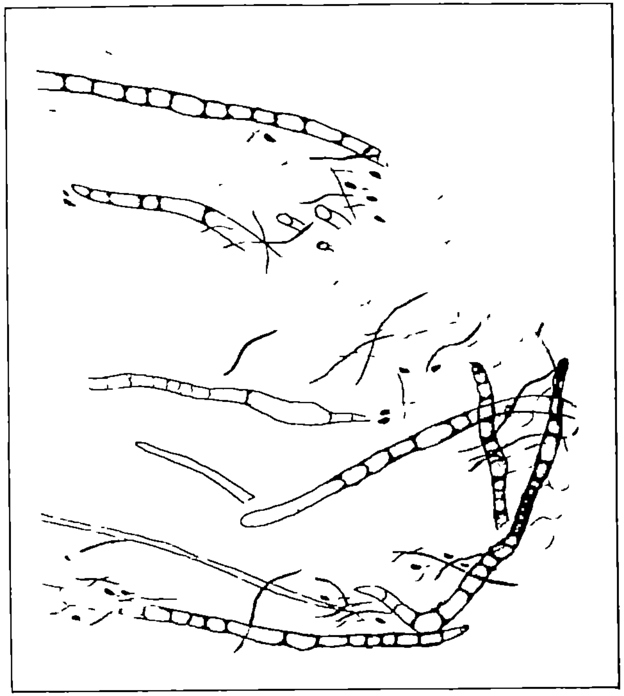

FIG 6

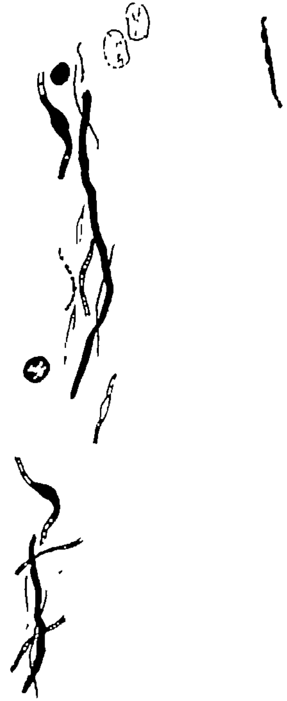

FIG. 7

infiltration of multinuclear leucocytes, while the former is not an acute irritative process, and the cells which make their appearance are mononuclear with a variable and usually abundant cell-protoplasm. The question whether a fibrinous subdural formation should be called inflammatory is largely a forensic one, which ultimately turns upon the connotation of the term inflammation, but the fact cannot be ignored that hæmorrhagic internal pachymeningitis presents important points of difference from acute fibrinous inflammations such as pneumonia.

Before concluding this section reference must be made to the granular deposit which is seen so frequently in subdural membranes, and which is exhibited in fig. 3. This material stains faintly by methylene blue, by Gram's method, and with hæmatoxylin, but with much greater distinctness by Weigert's fibrin stain. The individual granules have a diameter of $\frac{1}{2}\mu$ or less to 2μ, or even more, thus being very irregular in size. When unstained they have a yellowish-brown colour. They appear to be formed by fragmentation of red blood cells, an important preliminary to their ingestion by macrophages. In portions of membrane placed on agar at 35° C., and remaining sterile, they undergo no change.

Bacteriological Examination and Attempted Culture.

A bacteriological examination was made of twenty-three subdural membranes removed from the body at the end of from twenty-four to forty-four hours after death, the average period being thirty-three hours, an earlier section of the body not being permitted.

In all cases in which a bacteriological examination of, or attempted culture from, subdural membranes was undertaken precautions were of course taken to prevent accidental contamination. The instruments used in exposing and removing the skull-cap were previously sterilised in 5 per cent. carbolic lotion. During all manipulation care was taken to avoid unnecessary contact of the fingers with the scalp or skull. The dura mater was throughout brought solely into contact with sterilised instruments, and after its exposure all subsequent procedures were carried out with as much rapidity as possible. Whenever the dura mater was found to be adherent to the skull-cap further examination was abandoned, owing to the difficulty in such cases of avoiding accidental contamination. The dura being exposed two incisions were made and a flap reflected. With a sterilised Volkmann's spoon a portion of membrane of the size of a mustard seed to a hemp seed was quickly scraped off and transferred on the point of a platinum needle to the sloped surface of a peptone-agar tube, which was subsequently kept in an incubator at 35° C. Finally one or more pieces of membrane were scraped off and put into absolute alcohol to be subsequently examined for micro-organisms by staining methods. The pieces of membrane placed on agar, which at the end of about five days' incubation showed no growth, were then also hardened in alcohol, sectioned and stained for micro-organisms.

The result of the examination for bacteria, by Loeffler's and Gram's methods, of portions of subdural membrane hardened in alcohol immediately after removal from the body (Table I.), has with one exception been invariably negative, though a number of sections were carefully searched in each case. Such examination has been made in twenty successive cases [in Nos. 5, 7 and 22, the membrane was examined after incubation, see Table II.]. The exception just referred to is Case 14. Here there was probably accidental contamination, either prior to or at the time of autopsy. The micro-organisms found resembled in size and appearance bacillus coli communis and, like it, stained by Loeffler's but not by Gram's method. These micro-organisms were distributed sparsely over the sections without reference to any of its constituent parts, and thus had the aspect of *post-mortem* origin. This single exception does not afford an argument of value against the indication which the remaining nineteen cases furnish. It may, therefore, be concluded that bacteria are absent from subdural membranes during life.

Sections were in all the above cases stained for fungi by means of anilin-oil gentian-violet solution, followed by treatment with Gram's iodine solution and subsequent decolouration in a mixture of anilin-oil and xylol. Here again the result was invariably negative; no well-formed mycelial filaments, spores or conidia were found, though the fibrin filaments formed in recent subdural membranes, the nature of which has already been discussed,[1] were well stained by this method.

The portions of membranes placed upon peptone agar, and incubated at 35° C., sometimes remained sterile and sometimes developed colonies, as Table II. shows. Out of fourteen cases, in eight all the tubes remained sterile, while in six cases one or more of the tubes exhibited growth, the rest remaining sterile.

In all cases except the first two, a somewhat large amount of membrane, of the size of a mustard seed to a hemp seed or larger, was placed upon the agar in order that the growth of micro-organisms, if any were present, might continue in the membrane itself, which would naturally form a suitable medium. Inasmuch as each tube was implanted from a different area of the subdural membrane, it will be seen that the investigation is more extended than appears at first sight, for by counting the tubes enumerated in Table II. it follows that out of thirty-one pieces of membrane implanted on agar twenty-two remained sterile, while in eight micro-organisms grew.

When growth occurred upon the membrane placed upon agar, rarely more than a single colony appeared. In one tube a mould grew, together with a micro-organism resembling, in morphological staining and cultural characters, staphylococcus pyogenes albus; in other tubes, Fraenkel's pneumococcus, staphylococcus cereus albus and micrococci of doubtful nature respectively, made their appearance. From the multiplicity of the micro-organisms met with, their presence must be regarded as due to contamination subsequent to death, a possibility which is unfortunately present, owing partly to the length of

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[1] *Cf.* p. 186.

TABLE II.—SHOWING THE CONDITION OF THE MEMBRANES AND THE RESULTS OF ATTEMPTED CULTURE.

No. of Case.	Fibrin in Membrane (intra- and extra-vascular).	Bacteria in Sections of Membrane not used for Culture.		Bacteria in Sections of Membrane used for Culture (showing no Visible Growth).		Results of Attempted Culture.
		Loeffler's Method.	Gram's Method.	Loeffler's Method.	Gram's Method.	
1	[No sections cut.]	...	...	...	...	2 agar tubes; both showed numerous white colonies of micrococci or short bacilli.
16	Uniform filaments	None	None	...	...	1 agar tube sterile; 1, staphylococcus cereus albus.
15	Septate filaments	None	None	...	...	2 tubes sterile; 1, mould; 1, staphylococcus pyogenes albus.
8	Uniform filaments	None	None	None	None	1 agar tube sterile; 1, Fraenkel's pneumococcus.
22	Uniform and granular filaments	...	...	None	None	1 agar tube sterile; 1, micrococci in chains.
7	No filaments found	...	...	None	Micrococci	2 agar tubes. No visible growth. [See preceding column.]
5	No filaments found	...	...	None	None	2 agar tubes. No growth.
17	Uniform filaments	None	None	None	None	2 agar tubes. No growth.
18	Uniform filaments	None	None	None	None	2 agar tubes. No growth.
19	Uniform filaments	None	None	None	None	3 agar tubes. No growth.
20	Fine, uniform filaments	None	None	None	None	1 agar tube, 1 broth. No growth.
21	Fine, uniform filaments	None	None	None	None	2 agar tubes. No growth.
23	Fine, uniform filaments	None	None	None	None	2 agar tubes. No growth.
24	Very few filaments	None	None	None	None	2 agar tubes. No growth.

time elapsing before the autopsy was permitted to take place (the average period in Table II. was thirty-four hours after death), and partly owing to difficulties of technique. As regards the former it must be borne in mind that micro-organisms escaping from the intestinal tract may readily reach the cerebral sinuses by spreading along the blood contained in the caval and jugular veins.

That subdural membranes, however, are really free from micro-organisms during life is also highly probable from the large number of tubes remaining sterile, and this indication is further borne out by the circumstance that on the one hand the structure of the membranes exhibiting micro-organisms was in no essential particular different from that of the portions of membrame remaining sterile, while on the other hand the pus micro-organisms found in cases 16, 15 and 8 are well known to give rise, in living tissues, to a reaction which is quite different from that constituting a subdural membrane, and could not, therefore, have existed prior to death. Again, in every case except the first, in which microbes grew on a portion of membrane, another portion of the same membrane taken in a different situation remained sterile.

In eleven of the cases in which subdural membranes were placed on agar and incubated, such of the pieces as remained apparently free from growth were, at the end of five to seven days, hardened in alcohol, sectioned, and stained for micro-organisms, in order to avoid the possibility of overlooking growth. These pieces of membrane retained their colour without change, and stained well with hæmatoxylin. With one exception (7) they showed no bacteria. The fibrin filaments which they contained were in no way different from those found in the blood-vessels of portions of membrane which had not been incubated.

Reviewing the foregoing facts, all the evidence obtainable by staining methods, and from culture experiments, goes to show that subdural membranes during life are free from micro-organisms, and that the bacteria which were occasionally met with on portions of membranes incubated were due to *post-mortem* contamination.

Reports on Attempted Cultures from Subdural Membranes.

Case 1.—Pieces of membrane were implanted on two peptone-agar tubes, incubated at 35° C. In both tubes appeared numerous rapidly-growing, non-motile (in broth occasionally wriggling movements were seen) micrococci or short bacilli, rarely forming short chains, varying in size from ·6 μ to 1·5 μ, staining by Loeffler's but not by Gram's method, not liquefying gelatin, and rendering broth turbid. Nature of growth doubtful.

Case 16.—Pieces of membrane were implanted on two peptone-agar tubes, incubated at 35° C. One tube remained sterile. On the other appeared two colonies of staphylococci, 1 μ to 1·2μ in diameter, white on agar, potato and gelatin, which latter is not liquefied, and producing in broth a slight turbidity, with a whitish deposit at the bottom of the test-tube. Retained the stain by Gram's method. The micro-organisms, which on agar presented a waxy aspect, were identical with staphylococcus cereus albus.

Case 15.—Pieces of membrane were implanted on four tubes : two peptone agar, one potato, one broth. Incubated at 35° C. The potato and broth tubes showed no growth. On one agar tube a mould with a brown sporidium grew. On the remaining agar tube a staphylococcus 1 μ in diameter, staining by Loeffler's and Gram's methods, forming white or slightly brownish colonies on agar, white on gelatin (which was slowly liquefied) and potato, and causing in broth a slight turbidity with a whitish deposit. This microbe was thus, in morphological staining and cultural characters, identical with staphylococcus pyogenes albus.

Case 8.—Pieces of membrane were implanted on two peptone agar tubes, incubated at 35° C. One remained sterile. On the other a few extremely small colonies resembling droplets of dew appeared, consisting of diplococci, not definitely encapsuled, 1 μ in diameter, staining by Loeffler's and Gram's methods. No sub-cultures could be obtained. This micro-organism in the above characters resembles Fraenkel's pneumococcus.

Case 22.—Pieces of membrane implanted on two peptone agar tubes, incubated at 35° C. One tube remained sterile. On the other appeared a single colony, rapidly growing, consisting of micrococci, 1 μ in diameter, forming curved chains, staining by Loeffler's but not by Gram's method, yellowish-white on agar, brownish and abundant on potato, not liquefying gelatine, on which a film appeared, and forming also an abundant film on the surface of broth, which remained clear below. The nature of these micrococci is doubtful.

Case 7.—Pieces of membrane were implanted on two peptone agar tubes, incubated for five days at 35° C. Both appeared sterile. On sectioning the portions of membrane implanted, one was found to be free from micro-organisms, while the other contained staphylococci, staining by Loeffler's and by Gram's methods, and having a diameter of $\cdot 9\ \mu$ to $1\cdot 1\ \mu$.

[Towards the expenses of the following investigation a grant was made by the British Medical Association on the recommendation of the Scientific Grants Committee of the Association.]

Experimental Implantation of Subdural Membrane into the Subdural Space of Animals.

Portions of subdural membranes varying in size from a pin's head to that of a hemp seed, removed with the precautions already detailed, were placed in the subdural space of cats and dogs, being introduced through a small slit in the dura mater covering a cerebral hemisphere which had been previously exposed by trephining.

The operative procedures[1] were carried out with strict attention to asepsis. In every case the wound healed perfectly; no suppuration or other sign of sepsis occurred, and no micro-organisms were revealed by staining methods in sections made in the area of operation. No antiseptics were allowed to reach the membranes of the brain.

Other portions of the subdural membrane which remained over after implantation were sectioned and stained for micro-organisms by Gram's and Loeffler's methods. Cover-slip preparations of the fluid draining off from the membranes at the time of operation were also made. In no case were micro-organisms found.

Before proceeding to state the results of experimental inoculation it will be well to enquire what are the changes in the membranes of the brain of the animal inoculated which could be regarded as evidence of hæmorrhagic internal pachymeningitis. According to the resumé given in the first and second. chapters of this memoir, the earliest stages consist of swelling and multiplication of the nuclei on the inner surface of the dura mater, dilatation of the capillaries of the inner layer of this membrane and separation of fibrin, all these changes appearing, approximately at any rate, at the same time. Subsequently free cells make their appearance, together with fibroblasts and vasoblasts, and hæmorrhage very frequently occurs from the dilated capillaries. Among the free cells are many containing pigment masses derived from red blood cells.

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[1] I am indebted for assistance in the operative work to Professor Vaughan Harley, who very kindly permitted me to conduct the experimental portion of this investigation in his laboratory.

In any operation in which the dura is exposed and incised, as in the implantation of portions of subdural membrane beneath the dura mater, hæmorrhage into the subdural space is likely to occur. It is necessary, therefore, to distinguish between a blood pellicle resulting from mechanical injury during the operation, together with any changes which this effusion of blood subsequently undergoes, from a true progressive process such as occurs in internal pachymeningitis in the human subject. The condition resulting from subdural hæmorrhage after operative procedures has received the name traumatic hæmorrhagic internal pachymeningitis,[1] though it is not a true internal pachymeningitis, but merely a process of repair. In describing the experimental implantations of the subdural membrane (Table III.) an attempt is made to determine in advance the degree in which this factor is likely to influence the result by recording the amount of visible subdural hæmorrhage at the time of operation. Thus out of sixteen operations some subdural hæmorrhage was noted in five cases, very slight effusion of blood in four others, and none in the remaining seven. But such information is necessarily incomplete, since a certain amount of bleeding may possibly occur subsequently to the closure of the wound. There is here obviously a source of fallacy which requires to be borne in mind in estimating the effect of subdural implantation in setting up a true internal pachymeningitis. Traumatic hæmorrhage into the subdural space is not necessarily confined to the cerebral hemisphere opposite which the trephine aperture is made; the subdural space on the opposite side may also contain a thin layer of blood. Blood may also be effused into the sub-arachnoid space (Experiment 7), for in operating on a membrane so delicate as the dura mater of cats and dogs it is not always possible to avoid injuring the pia mater.[1]

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[1] Sperling, "Experimente zur Frage der Pachymeningitis," *Centralbl. f. die medic. Wissensch.*, 1871. H. Laurent, "Zur Histogenese der Pachymeningitis hæmorrhagica interna" (five plates), *Inaug. Dissert.*, Düsseldorf, 1898. Van Vlenten, "Ueber Pachymeningitis hæmorrhagica interna traumatica," *Inaug. Dissert.*, Bonn, 1898.

Another source of fallacy in the experimental implantation of subdural membrane arises from injury to the membranes of the brain (apart from hæmorrhage) occurring during operation. This may readily be supposed to be capable of producing such changes as swelling of nuclei and dilatation of blood-vessels, which are among the earliest changes to occur in hæmorrhagic internal pachymeningitis occurring in the human subject. With the view of eliminating the influence or possible influence of injuries inflicted during operation, two precautions were taken. In the first place, in judging of the effect of experimental implantation in producing an internal hæmorrhagic pachymeningitis, no note is taken of the marked changes, chiefly of a reparative character, occurring in the immediate neighbourhood of the implanted membrane and the sutures in the dura mater. It is inevitable that changes in this situation, unless so striking and considerable as altogether to exclude the sole influence of simple trauma, must be disregarded, and attention be specially directed to changes occurring outside the actual area of operation. In the second place, a series of control operations was made in which the procedure was identical with that practised in the implantation experiments with fresh subdural membrane, except that the pellicle employed had previously been sterilised by immersion for three weeks in absolute alcohol, followed by three minutes' boiling in water immediately before insertion. Of the former experiments eight were made, and the control experiments were the same in number.

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[1] Hæmorrhage into the subdural and sub-arachnoid spaces may occur subsequent to death, as in Experiments 3, 7 and 9. Decapitation is to be avoided, as this commonly leads to such hæmorrhage, spreading upwards and downwards from the site of injury. Hæmorrhage from rupture of distended surface veins during removal of the brain is not always avoidable. The liability to its occurrence is lessened by bleeding the animal before removing the brain.

The results of this double series of experiments are given in Table III, arranged, for convenience of reference, not in the order in which they were made, but according to the occurrence of change in the dura mater or subdural space. As a rule the animals were kept alive for from eighteen to twenty-six days, but two were kept for fourteen weeks. The source of the membrane used, which was obtained from four necropsies, is stated in the case of the first series, and by reference to Tables I. and II. it will be noted that staining methods showed the absence of bacteria, while portions of the membranes used, placed on agar at the time of *post-mortem* examination, also remained sterile. In all but two (Experiments 7 and 8) of these cases the membrane used exhibited intravascular filaments. As an appendix to this section a short account of each individual experiment is given.

After the operation the animals showed no ill effects attributable to the subdural implantation. The wound in every case healed by first intention without any sign of sepsis. Seven of the animals (Experiments 4, 8, 9, 11, 12, 13, 16) subsequently did not take their food well, or exhibited other indication of impairment of general health, accompanied by sneezing and a running from the nose. After death in these cases the mucous membrane of the frontal sinuses was found to be reddened and swollen, and the frontal sinuses in some cases contained clear or blood-stained fluid. Other animals, not operated upon, also suffered from the same coryzal condition. In four (Experiments 1, 7, 11, 14) of the animals operated upon, a subcutaneous false bursa formed, varying in size from a shilling to a threepenny-bit, the walls of which were smooth and usually blood-stained, while the cavity in one case contained a few clots of blood, remaining empty of clot or fluid in the remaining cases. It is clear that these subcutaneous false bursæ, at the site of the operation wound, formed as the result of the movements of the animal during the process of healing.

The microscopical examination of the dura mater and pia-arachnoid of cats and dogs is necessarily difficult owing to the extreme thinness of the membranes. Their investigation after experimental implantation has therefore required a considerable amount of patient and careful work. The hardening agent employed was in all cases alcohol, and paraffin embedding was used. The sections of dura and pia were usually oblique, but transverse sections were also made. The staining methods employed included in every case, v. Gieson's, Loeffler's, Gram's, Weigert's (fibrin) and Unna-Taenzer's (elastin). The dura and pia were examined at the site of implantation, at some distance from the trephine aperture on the side of operation, and on the opposite side.

The changes actually met with in the meninges of the animals operated upon were, in fact (except in the immediate area of implantation), few in number and slight in degree. In describing the results of experimental implantation, it will be convenient first to take the changes induced in the area of operation, and next the condition of the meninges at some distance from the trephine hole. The latter changes will be described first irrespectively of the nature (sterile or otherwise) of the membrane implanted, and subsequently a comparison made between the results of the control and of the actual experiments. This again will necessitate a further comparison between post-experimental changes and those constituting human hæmorrhagic internal pachymeningitis.

At the site of implantation the dura, at the end of about three weeks, was found adherent externally to the temporal muscle and internally to the membrane inserted, and to the pia-arachnoid all round. The muscle fibres adherent to the dura were striated faintly longitudinally, but had for the most part lost their transverse striation and presented a hyaline aspect; their nuclei were increased. Some of the fibres were much atrophied. The portion of false membrane inserted had lost its translucent, grey, œdematous, hæmorrhagic character, was much smaller, drier and more opaque, and had assumed a brownish colour. Sometimes no trace of the membrane could be found. On microscopical examination the remains of the membrane, when present, consisting of a small amount of débris, showed no definite structure, staining darkly and diffusely (with hæmatoxylin and methylene-blue). There was an abundant infiltration of cells, some with single, some with partite nuclei, possessing a variable amount of cytoplasm. Pigment cells were very rarely seen. Lying between the cells in great profusion were collagen bundles, which, blending with the dura and pia, made the latter membranes difficult to distinguish. Lying upon the cortex was much fairly loose fibroid tissue, somewhat resembling that of the human pia-arachnoid when thickened over atrophied brains, but coarser and not so richly provided with cells, and not exhibiting a profusion of blood-vessels. The endothelial cells which form so striking a layer in the normal pia-arachnoid were absent. Few or no pigment cells were found. These changes were most marked at and about the sutures in the dura, and further outwards gradually merged into the normal condition of the meninges, or became continuous with the slighter changes about to be described as occurring over the more distal portions of the cerebrum. At the site of implantation the tissues were of a slightly brownish-grey colour, but no definite yellow staining was noted. The cerebral cortex opposite the area of operation showed usually surprisingly little change. The different layers of cells usually showed no obtrusive alteration in aspect, and the molecular layer was in some of the animals apparently unchanged. In other animals, however, there were changes in the first layer of the cortex; it presented opposite the implanted membrane a somewhat vacuolated character; occasionally mononucleated or multinucleated cells penetrated within it for a short distance and in small numbers; sometimes, again, some of the vessels descending into the cortex exhibited a perivascular cell-infiltration for a short distance, or the vessel walls were thickened and tinted readily with stains; and, finally, in three cases collagen bundles had descended into the molecular layer. A small amount of yellow softening, visible to the naked eye, was not uncommon. In all these cases the pia had evidently been injured at the time of operation. In one case the membrane used had been inserted, in part at any rate, into the sub-arachnoid instead of the subdural space. The neuroglial feltwork covering the cortex did not appear to have undergone any increase. Careful examination failed to reveal the presence of fibrin-like filaments in the vessels or elsewhere. In the two animals kept fourteen weeks after operation it was difficult to recognise with certainty any remains of the membrane implanted, fibrosis was more advanced and fewer cellular elements were seen. As already stated, in no case were micro-organisms found in the area of operation.

In the meninges lying outside the immediate area of operation the changes found were, in contrast to those present in this area, few in number and slight in degree.

In most, but not all cases (ten out of sixteen), the nuclei of the inner layer of the dura were well defined (Experiment 5), of large size (Experiments 13 and 14), or distinctly swollen (1, 2, 3, 6, 7, 9, 11). The endothelial and other nuclei of the pia arachnoid were, in the same cases, unusually distinct, though their appearance was generally less striking than those of the dura. The nuclei of the normal dura and pia of cats and dogs vary in character in different sections, but are usually of a very flattened or even shrivelled aspect, in contrast to their fulness in the cases enumerated above. This change in character, occurring as it did at a distance from the trephine area, presumably was the consequence of the operative interference, and was accompanied by the other changes described below. The alteration in the dural nuclei was, however, confined to an increase in size; no increase in number occurred. In the case of the pia arachnoid the nuclei normally visible were variable both in aspect and number, and it was therefore more difficult to recognise an increase in number. It can, however, be confidently affirmed that

TABLE III. — SHOWING THE RESULT OF IMPLANTATION BENEATH THE DURA MATER OF SUBDURAL MEMBRANES, NON-STERILISED AND STERILISED.

No. of Experiment.	Animal.	Inoculated with	Hæmorrhage beneath Dura during Operation.	Animal Killed at end of	Naked-eye Characters.	Microscopic Characters.
1	Cat	Recent membrane. Case 24	Present	19 days	Reddish-brown pellicle, yellowish in places, on inner surface of dura over cerebrum	Free cells, some pigmented, on inner surface of dura, together with blood.
2	,,	Recent membrane. Case 24	Present	19 ,,	Reddish brown subdural pellicle	Free cells, some pigmented, on inner surface of dura, together with blood.
3	,,	Recent membrane. Case 20	None	21 ,,	Recent subdural extravasation of blood (during removal of brain)	No free cells in subdural space. Thin layer of blood on inner surface of dura.
4	,,	Recent membrane. Case 20	None	14 weeks	No subdural pellicle	Free cells, some pigmented, on inner surface of dura.
5	,,	Recent membrane. Case 18	Present	19 days	,, ,,	No free cells in subdural space. Inner surface of dura stains yellow.
6	,,	Recent membrane. Case 18	None	19 ,,	,, ,,	No free cells in subdural space. Inner surface of dura stains yellow.
7	,,	Recent membrane. Case 5	None	18 ,,	No subdural pellicle. Slight extravasation of blood into sub-arachnoid space during removal of brain	No free cells in subdural space. Opposed surfaces of dura and pia stain yellow. Blood extravasated in sub-arachnoid space.
8	,,	Recent membrane. Case 5	None	18 ,,	No subdural pellicle	No free cells in subdural space.
9	Dog	Sterilised membrane	None	26 ,,	Dark red subdural pellicle (produced by decapitation)	No free cells in subdural space. Altered blood on inner surface of dura.
10	,,	,, ,,	Very slight	19 ,,	No subdural pellicle	A few free cells, some pigmented, in subdural space. Unaltered blood on inner surface of dura.
11	Cat	,, ,,	Very slight	26 ,,	Brownish-red subdural pellicle	Very few pigment cells in subdural space. Amorphous material between dura and pia.
12	,,	,, ,,	Present	21 ,,	No subdural pellicle. Dura and pia over cerebrum of yellowish tint	No free cells in subdural space. Dura and pia stained yellow.
13	,,	,, ,,	Present	14 weeks	No subdural pellicle. Dura over cerebrum light yellow	No free cells in subdural space. Dura and pia stained yellow.
14	,,	,, ,,	Very slight	18 days	No subdural pellicle	No free cells in subdural space. Inner layer of dura stained yellow.
15	,,	,, ,,	None	19 ,,	,, ,,	No free cells in subdural space.
16	,,	,, ,,	Very slight	26 ,,	,, ,,	No free cells in subdural space. In places, yellow staining of inner surface of dura.

no clearly recognisable increase occurred outside the trephine area after experimental interference. In two cases (Experiments 6 and 10) the granules of the mast cells of the dura were stained, but in all the remaining cases these granules had been discharged.

In the subdural space a blood pellicle in four cases (Table III.) was recognisable on inspection, and could be scraped off the membranes. In two of these, however (Experiments 3 and 9), the pellicle resulted from hæmorrhage occurring during decapitation, and the blood effused was unaltered, or very slightly changed, and in particular was free from cells; these pellicles, therefore, had no relation to the operation. In the remaining two cases (Experiments 1 and 2), in which hæmorrhage was observed to occur at the time of operation, and it was feared that the amount was not inconsiderable, the pellicles were darker and more brownish in tint, the outlines of the red cells were not always recognisable, and in places the layer of blood presented an eroded appearance. In addition free cells were found in the substance of the pellicle. These were usually provided with a single rounded nucleus, staining darkly when small and more lightly as their size increased, and were surrounded by a variable amount of cytoplasm. There were, however, also cells with irregular or partite nuclei. A few of the cells present contained pigment masses of a yellowish-brown colour. Good plasma staining could not be obtained, nor were most cells met with in the subdural space. Some difficulty was at times experienced in making out the characters of the cells, owing to the dark colour of the subdural pellicle. Capillaries were met with infrequently in the blood film; their contents were free from fibrin filaments. No collagen bundles could be defined in the subdural layer. It is clear that the latter two pellicles (Experiments 1 and 2) had their origin in blood effused into the subdural space, as a result of the operative procedure. In another case (Experiment 11) a thin pellicle formed, which presented an opaque character, and did not stain yellow by v. Gieson's method. No red blood cells were recognisable in it, though a few free cells not containing pigment were noted.

In two other cases (Experiments 12 and 13) the dura mater presented a yellowish colour, and at first sight it was thought that a subdural pellicle had formed. On scraping the inner surface of the dura, however, no pellicle could be removed, and the aspect of the dura remained unaltered. On microscopical examination it was found that the inner layer of the dura stained yellow by v. Gieson's method. There was, however, no blood film on the dura, which, except for the altered staining reaction of the collagen bundles of its inner layer and the large size of its nuclei (Experiment 13 only), was unchanged in character. In both these cases subdural hæmorrhage had been produced at the time of operation by tearing across the fine vessels passing from dura to pia arachnoid, so that at the conclusion of the operation blood was present in sufficient quantity in the subdural space to prevent the brain from being seen through the dura. The circumstance that no blood pellicle formed seems to be explicable on the assumption that hæmolysis of the blood effused into the subdural space occurred, leading to absorption without cell invasion, but causing staining of the dura and altering its reaction to dyes. In both these cases the pia arachnoid also stained yellow by v. Gieson's method; owing to its lesser thickness its staining was not so conspicuous as was that of the inner layer of the dura.

In five other cases (Experiments 5, 6, 7, 14, 16) the membranes which did not appear markedly tinted when examined with the naked eye, were stained yellow by v. Gieson's method. In each case the dura was so stained, and in two cases the pia also, while in one case the adjoining part of the molecular layer of the cortex was also tinted. In these cases no pellicle was present in the subdural space, nor were any pigment cells seen. The explanation of this staining appears to be the same as that already given, namely, that effusion of blood originally occurred upon or near the membranes which subsequently stained, hæmolysis then taking place, and the tissues all round being stained, as occurs in the skin lying over a subcutaneous blood extravasation. In the two cases in

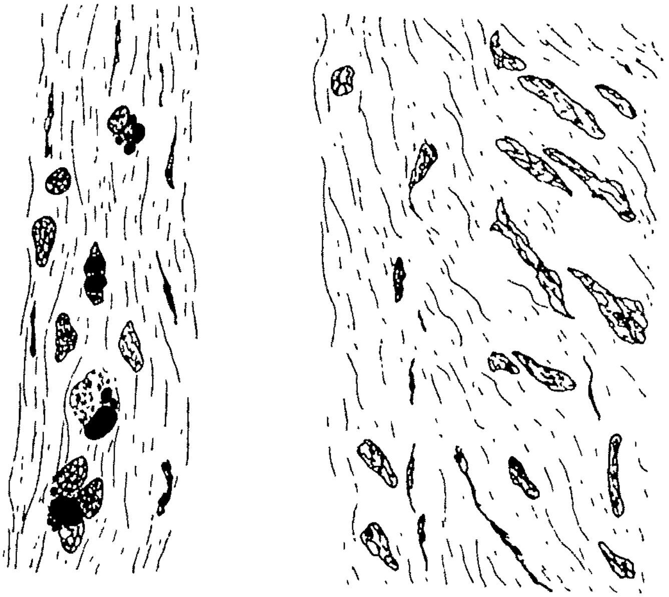

FIG. 8.

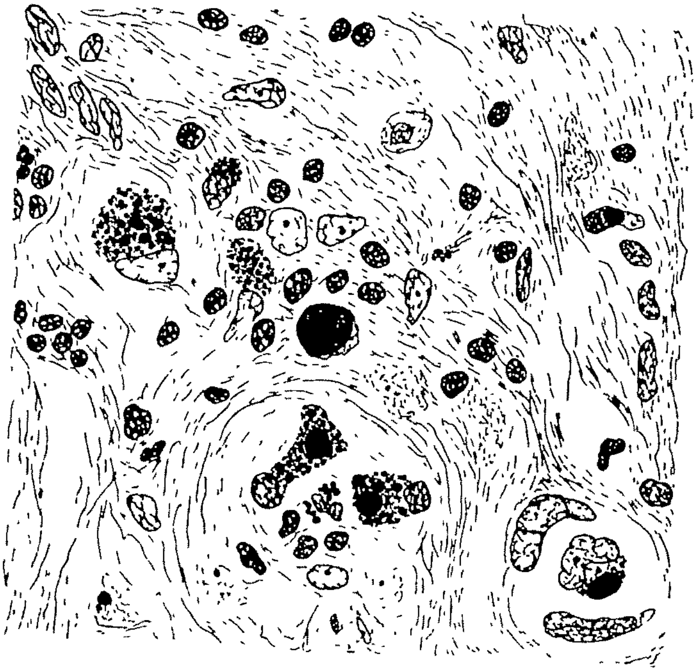

FIG. 9.

which subdural pellicles had formed before the animals were killed; no yellow staining of the inner layer of the dura or of the pia-arachnoid took place by v. Gieson's method.

In the subdural space free cells occurred in the blood film which formed in two cases subsequently to operation (Experiments 1 and 2), as already described. In Experiments 4, 10 and 11, a few pigment cells were found here and there in the subdural space, and were accompanied by free cells (figs. 8 and 9). The latter were irregularly distributed, were very few in number, not forming a distinct layer, and the meninges, it will be noted, were not stained yellow by v. Gieson's method. A good idea of the appearance of the free cells is afforded by the figures just referred to.

Beyond the above changes there is nothing further to note in the membranes of the brain, or the subdural space after the operative procedure. There was no vascular dilatation observable. A very careful search failed to reveal any separation of fibrin either at the site of implantation or at a distance therefrom. There was a development of fibrous tissue in the trephine area only, not elsewhere. In Experiments 1 and 2 there were a very few capillaries in the subdural pellicle, but none formed in the extra-implantation area in any of the remaining experiments.

To sum up, the changes found over the brain after operation were limited (excluding the events occurring in the actual area of operation) to (1) swelling of the nuclei of the membranes of the brain, chiefly in the inner layer of the dura mater (10 Experiments), (2) the formation of a subdural blood pellicle (5 Experiments), (3) yellow staining of the membranes visible to the naked eye or revealed by v. Gieson's method (7 Experiments), and (4) the appearance of free cells pigmented or otherwise in the subdural space (5 Experiments), rarely accompanied by a few new capillaries (in Experiments 1 and 2).

Comparing these changes with those occurring in the human subject, it will be seen that in no case has a progressive process been started spreading from the site of implantation. An increase in size of the nuclei of the inner layer of the dura occurred, it is true, at a distance from the site of implantation, but no increase in number of these nuclei took place, no dilatation of the capillaries of the inner layer of the dura occurred, no separation of fibrin was noted, and no subdural pellicle at all comparable to that occurring in human hæmorrhagic internal pachymeningitis. Furthermore, except at the site of implantation, where processes of repair were set up, no new formation of fibrous tissue occurred in the subdural space. Recent subdural hæmorrhages, which form so striking a feature of the process occurring in the human subject, were absent.

It remains now to be considered whether the changes met with bore any relation to the insertion of sterilised in place of non-sterilised membrane. A review of the experiments reveals the fact that changes outside the trephine area occurred more frequently when non-sterilised membrane was inserted, but were not confined to these cases. Thus, swelling of the nuclei of the inner layer of the dura occurred in all but two (Experiments 4 and 8) of the first series in which non-sterilised material was used, but only in four of the control experiments. A subdural blood pellicle formed prior to death in two (Experiments 1 and 2) of the former, but not in any of the controls: Free cells were found in the subdural space in Experiments 1, 2 and 4 of the first series, and in Experiments 10 and 11 of the second series. It is clear, therefore, that though changes occurred in the cerebral membranes of the sixteen animals operated upon more frequently when non-sterilised membrane was used, yet such changes can also occur after pure control operations, and are therefore not in any way distinctive of the former. It is true that a blood pellicle occurred after operation only in two of the first series. This led me at first to suspect that a true hæmorrhagic pachymeningitis had occurred, but further observations dispelled this view, though an attempt to reproduce this condition in two of the controls (12 and 13) failed, apparently owing to hæmolysis occurring in the blood effused. Why hæmolysis should occur in some cases but not in others is not easy to explain. It is well known that the injection of the blood of one animal into the veins of another may lead to hæmolysis,[1] and this factor may have been effective in setting free hæmoglobin in the first series of experiments, but such a suggested explanation may not apply to the second series, in which sterilised membrane was employed.

A fact which is not brought out in Table III., but which has an important bearing upon the causation of the changes found after operation, is the circumstance that these latter are less marked the less the trauma, and thus tend to become few or absent in the later experiments, in which greater facility of operation had been acquired. Three of the changes occurring outside the trephine area, namely, the formation of a blood pellicle, the presence of free cells in sparse numbers, pigmented or not, and yellow staining of the membranes, are changes which necessarily follow the effusion of blood sub dura resulting from operation. The swelling of the nuclei of the membranes may possibly have some relation to the same event. It was, however, absent in Experiment 12, in which yellow staining was visible to the naked eye. Perhaps the occurrence of nuclear swelling is not of great importance; I have met with it in the dura of a cat, not operated upon, which appeared quite healthy at the time it was killed. As already mentioned, most of the animals exhibited redness and swelling of the mucous membrane of the frontal sinuses, but it is not at all clear that this was a factor in changing the aspect of the nuclei of the inner layer of the dura.

In the implantation area reparative changes occurred, consisting of the formation of an abundance of connective tissue, in the meshes of which free cells occurred. The appearance in section did not differ markedly from that ordinarily noted in aseptic operation wounds, and the cases in which non-sterilised membrane was employed differed in no essential particular from those in which the membrane inserted had been previously sterilised. There were very few pigment cells recognisable in and about the implantation area, dilated vessels were not encountered, fibrin was not formed, hæmorrhages were not met with, and there was no appearance of œdema. It is obvious, therefore, that no process occurred in the implantation area which could with propriety be compared to human hæmorrhagic internal pachymeningitis.

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[1] C. P. W. Bullock, "Recent Work on the Nature of Hæmolysis," *The Practitioner*, London, 1900, vol. 65, pp. 672, 683; also 1901, vol. 66, pp. 499-516.

The results of the implantation of subdural membrane beneath the dura of animals, in the eight experiments here described, have been, therefore, entirely negative, so far as the production of a progressive hæmorrhagic process comparable to that occurring in the human subject is concerned. The changes occurring, with the doubtful exception of swelling of the nuclei of the inner layer of the dura, and less frequently of the pia-arachnoid also, resulted from or followed upon subdural hæmorrhage occurring at the time of operation. To the condition found in Experiments 1 and 2, the term traumatic internal pachymeningitis has been given, but the term as applied to what is comparable to a simple process of repair is to be deprecated.

It must, however, be observed that the brains of the animals employed were quite healthy, while in the cases recorded in Table I., from which the subdural membranes were obtained, there was more or less wasting of the brain mantle, with correspondingly marked changes in the meninges and excess of fluid in the sub-arachnoid and ventricular spaces. Implantation of a portion of a false membrane cannot be expected to reproduce hæmorrhagic internal pachymeningitis unless this process is an infective one, and even in this case it may conceivably be unable to set up the morbid process except in a brain which is atrophied. If, however, hæmorrhagic internal pachymeningitis is a process dependent upon the separation of fibrin, due to altered metabolism of brain tissue not forming part of an infective process, as appears to be indicated by the observations recorded above, then such implantation necessarily fails to set up a progressive process of membrane formation.

SUMMARY.

The observations recorded in the preceding may be briefly summarised as follows:—

(1) Intravascular separation of fibrin is an apparently constant event in subdural membrane formation.

(2) Subdural membranes are free from micro-organisms as revealed by staining methods. The results of attempted culture upon agar, though not always negative, indicate that during life such membranes are free from bacteria.

(3) Experimental implantation of false membrane into the subdural space of cats fails to set up a progressive process of membrane formation. The few changes which occur outside the operation area are comparable to a process of repair.

Finally, the view may be advanced that pachymeningitis hæmorrhagica interna is a morbid process, in which the essential lesion is a separation of fibrin, usually within the blood-vessels upon which the other changes in this condition are largely if not chiefly dependent.

DESCRIPTION OF EXPERIMENTS.

Experiment 1.—A cat was trephined over the left cerebral hemisphere and the dura mater exposed. All hæmorrhage having been arrested, a small opening was made into the dura and a portion of subdural membrane, about as large as a mustard-seed, obtained twenty-four hours previously from Case 24 (Tables I. and II.), introduced between dura and pia. (During the interval between the autopsy and the operation the subdural membrane was preserved in a sterilised test-tube plugged with cotton-wool, at a temperature of about 20° C.) The dura was then sutured and the wound closed. Throughout the operation careful attention was paid to the maintenance of asepsis, and the portions of membrane remaining over were implanted on agar, no growth of bacteria occurring (Table II.). Blood in not inconsiderable amount was effused into the subdural space at the time of the operation.

The animal showed no ill effect after the operation, its general condition not being altered. At the end of nineteen days it was killed. The external wound was then completely healed, no appearance of suppuration being noted. Beneath the skin a false bursa had formed, the walls of which were blood-stained and the cavity of which contained a little blood-clot. The dura mater presented on its inner surface, over both hemispheres, and also, less marked, over the cerebellum, a thin-reddish-brown pellicle. The pia arachnoid was also a little reddened. In this, as in the succeeding experiments, the remains of the membrane introduced at the time of the operation were found much reduced in size, changed to a brownish-grey opaque mass, adherent to both dura and pia.

On microscopical examination a layer of altered blood, varying in thickness from about 25μ downwards, was found on both sides adherent to the dura mater, covering the cerebrum. Frequently this presented an eroded appearance on its outer surface in contact with the dura, where occasionally capillaries could be recognised. Lying upon and within this blood-pellicle, in which red cells with more or less altered outlines were recognisable, mononucleated cells were found, exhibiting a very variable amount of protoplasm; some of the larger of these cells contained, sometimes in large amount, reddish-brown pigment evidently derived from red cells. No dilated blood-vessels were seen in the pellicle or in the inner layer of the dura mater. No fibrin filaments were discovered. The nuclei of dura and pia were swollen, but were not, apparently, increased in number. The dura mater did not show any tendency to yellow staining of its inner layer by v. Gieson's method. Staining methods failed to reveal the presence of bacteria.

The wall of the false subcutaneous bursa was composed of areolar tissue containing in places muscular fibres, infiltrated irregularly with small cells, mostly mononucleated, some containing blood pigment. No micro-organisms were seen.

The portion of subdural membrane implanted formed an amorphous mass, much fragmented, staining deeply and diffusely with hæmatoxylin and with methylene blue, embedded in fibroid tissue rich in cells with single, horseshoe-shaped or partite nuclei, and more or less rich in cell protoplasm, those of the plasma-cell type predominating. Pigment cells were also met with, but were not common. In the immediate neighbourhood of the fragments of implanted membrane a few giant cells were seen surrounding or applied to the remains of the membrane. In the neighbourhood of these remains the dura and pia fused together, so that the latter could be recognised with difficulty, and the cortex of the cerebrum was for a short distance altered by the disappearance of part of the natural structure of its molecular layer, which here presented an eroded aspect and was penetrated by free cells with single or partite nuclei, while in some situations strands of fibrous tissue penetrated the cortex. Opposite the implantation area the cortical vessels were in places thickened and the seat of a marked perivascular infiltration of plasma cells. Among the muscle fibres adherent to the dura externally a plasma-cell infiltration was also found. No micro-organisms were found by Gram's and Loeffler's methods in or about the implanted membrane.

This description of the appearances in the area of operation applies without any important modification to the remaining animals operated upon, and will not therefore be further repeated in detailing the results of individual experiments. In Examples 4 and 13 there was much more fibrosis and less cell infiltration at the site of implantation than in the other experiments, and the remains of the membrane could not be recognised with certainty.

Experiment 2.—Cat. Operative procedure as before. Effusion of blood beneath the dura was noted at the time of operation. The subdural membrane used in this as in the preceding experiment was obtained twenty-four hours previously from Case 24, and exhibited no growth of bacteria when implanted on agar (Tables I. and II.).

The animal, which exhibited no ill-effect after the operation, was killed at the end of nineteen days. The external wound had completely healed, and no subcutaneous false bursa had formed. A small amount of exudation was noticed at the lower portion of the trephine aperture, around a piece of wax used for arresting hæmorrhage from the diploe. The opening in the dura had healed, and was adherent to the structures with which it was in contact. The inner surface of the dura was of a reddish-brown tint, especially above the left frontal lobe and on the under surface below both frontal lobes. The remains of the membrane implanted were of an opaque greyish-brown colour, adherent to the dura and pia, which had coalesced for a short distance all round.

On microscopical examination, external to the trephine area, altered blood was found lying upon the dura in a layer of 30μ or less thick, and penetrating between its fasciculi. The individual red cells were in some places little altered in shape, in other places they were much distorted, while sometimes their outlines were indistinguishable, or again they were replaced by yellowish-red granules 1μ to 2μ in diameter. Upon and within this collection of blood were free cells sparsely scattered, mostly mononucleated, exhibiting sometimes little sometimes abundant protoplasm. Many of the cells contained reddish-brown pigment. Very few capillaries were seen in the pellicle, and no dilated vessels in the inner layer of the dura or elsewhere. No fibrin filaments could be discovered. The proper nuclei of the dura and pia were increased in size, but did not appear to be increased in number. There was a slight tendency to yellow staining, by v. Gieson's method, of the inner layer of the dura. On staining by Loeffler's and Gram's methods no bacteria were found in any of the sections. The exudation round a fragment of wax, referred to above, was made up of plasma cells. No micro-organisms were present in this exudation.

Experiment 3.—Cat. Operative procedure as before. No blood was observed beneath the dura at the time of operation. The subdural membrane inserted was of the size of a hemp-seed, and was obtained about twenty-four hours previously from Case 20. When placed upon agar no growth of bacteria occurred (Tables I. and II.).

No untoward circumstance followed the operation, and the animal was killed at the end of twenty-one days. The wound was perfectly healed, and no subcutaneous false bursa was present. There was some staining of the tissues in the area of operation, which exhibited no sign of inflammatory reaction. The inner surface of the dura was reddened over both cerebral hemispheres at vertex and base, and there was a thick layer of recent blood-clot over the medulla and adjoining part of the spinal cord, produced during decapitation shortly after death. The remains of the membrane implanted were pale brown in colour, and reduced in size; adhesions of the membranes were found in the neighbourhood.

Outside the implantation area the nuclei of the inner surface of the dura and those of the pia-arachnoid were somewhat swollen, but were not increased in number. There was a thin layer of altered blood, in which it was difficult to recognise red blood-cells, frequently only granular matter of a yellowish-brown colour being seen, lying upon the pia-arachnoid, but no free cells beyond a very small number of multinuclear leucocytes, evidently derived from the effused blood, were seen, nor did any pigment cells make their appearance in the sections. The pia-arachnoid stained slightly yellowish by v. Gieson's method. No dilated blood-vessels were seen, nor were any fibrin filaments recognisable. The absence of new cells, taken by itself, indicates that the blood in the subdural space was effused during decapitation.

Experiment 4.—Cat. Operation as before. No blood escaped beneath the dura at the time of operation. The subdural membrane was from the same source as in the preceding experiment, and was inserted at nearly the same time after removal from the body.

The animal showed no ill-effect from the operation, but two weeks later it suffered from an attack of coryza. It was killed at the end of fourteen weeks. The dura mater then appeared perfectly healthy; it had a dead white colour and exhibited no yellow staining. The pia-arachnoid was also unchanged. The mucous membrane of the frontal sinuses was reddened. The membrane implanted had become pale brownish in colour and was reduced in size. It was adherent to dura and pia, and opposite it the cortex showed some yellow softening.

On microscopical examination the nuclei of the dura generally, but mostly of its inner layer, were found to be slightly swollen over the vertex on both sides. No increase in number of these nuclei was noted. No distinct subdural pellicle was present, but free cells, generally mononucleated, occasionally with multipartite or horse-shoe nuclei, with a variable amount of protoplasm, sometimes containing blood-pigment, were found both on and within the inner layer of the dura, and in a few places a very thin layer of altered blood was recognisable over a small area of the membrane. By v. Gieson's method there was no yellow staining of the inner layer of the dura. The nuclei of the pia-arachnoid did not appear to be increased in number. There were no dilated vessels, and no fibrin filaments were present.

No bacteria were found in any of the sections on staining by Loeffler's and Gram's methods.

Experiment 5.—Cat. Operative procedure as before. There was a small escape of blood under the dura at the time of operation. The subdural membrane used was obtained about twenty-two hours previously from Case 18, and exhibited no growth of bacteria when incubated on agar (Tables I. and II.).

The animal exhibited no ill-effect from the operation, and was killed at the end of nineteen days. The wound was then perfectly healed; no subcutaneous bursa was present. The dura mater appeared quite natural. There was no subdural pellicle. The pia-arachnoid was slightly congested. The portion of membrane inserted beneath the dura was difficult to recognise; the meninges in its neighbourhood were adherent.

The nuclei of the dura mater were somewhat swollen on its inner surface, which in places stained yellow by v. Gieson's method.

There was no subdural pellicle, nor were any pigment cells seen. The nuclei of the pia-arachnoid were well defined, but were not increased in number. No dilated vessels were noted, nor could any fibrin filaments be demonstrated.

The sections examined gave, by Loeffler's and Gram's methods, no evidence of bacteria.

Experiment 6.—Cat. Operative procedure as before. No blood passed beneath the dura at the time of operation. The subdural membrane was from the same source as in the preceding experiment.

The animal exhibited no ill-effect after the operation. It was killed at the end of nineteen days. Union of the edges of the wound was complete, and no subcutaneous bursa had formed. The dura mater and pia-arachnoid were quite natural in aspect, and no subdural pellicle was seen. The débris of the membrane placed in the subdural space were of a brownish colour, and were adherent to dura and pia.

On microscopical examination some of the nuclei of the inner layer of the dura and of the pia, outside the trephine area, were found to be swollen, but did not appear to be increased in number. The inner layer of the dura was stained deeply yellow by v. Gieson's method. Some of its basophile cells retained their granules. No free cells were recognisable in the subdural space, and no cells containing pigment were present. The nuclei of the pia-arachnoid were flattened, and were oval or irregular in outline, without clearly recognisable cytoplasm. There were no nuclei which were free from flattening, and no partite nuclei were seen. The capillaries in the molecular layer of the cortex were slightly distended, and their walls were slightly thickened and stained with unusual distinctness.

The sections were free from bacteria.

Experiment 7.—Cat. Operative procedure as before. A piece of subdural membrane of the size of a small pea, obtained twenty-two hours previously from Case 5, was inserted under the dura. Implanted on agar, no growth of bacteria occurred. No blood was noted under the dura at the time of operation.

The animal recovered completely from the operation, and was killed eighteen days later. The external wound was then completely healed. There was a small false bursa of the size of a threepenny-bit beneath the integument, the walls of which showed some blood-staining. The dura over the cerebrum was slightly congested; the pia remained of natural aspect, and no pellicle could be discovered. The membranes covering the cerebellum were normal. There was some effusion of blood into the sub-arachnoid space, occurring during decapitation. The remains of the membrane implanted were grey in colour and adherent to the surrounding structures.

The inner layer of the dura mater stained by v. Gieson's method of a deep yellow, as did also the superficial layer of the pia. In some situations a thin layer of blood was found in the sub-arachnoid space, the outlines of the red cells being usually ill-defined. The nuclei of the inner layer of the dura and of the pia were larger than usual, but no increase in number of nuclei was noted, and no free cells, pigment-holding or otherwise, were found in the subdural space. From the absence of free cells, and in particular of pigment cells, it follows that the layer of blood effused was produced subsequent to death. It represents the hæmorrhage into the sub-arachnoid space during decapitation. There were no dilated vessels in the dura, and no fibrin filaments could be found.

No bacteria were recognisable by Loeffler's or Gram's methods in any of the sections.

Experiment 8.—Cat. Operative procedure as before. No blood was effused beneath the dura at the time of operation. The subdural membrane was from the same source as in the preceding experiment, and was inserted at nearly the same period after removal.

The animal exhibited no ill effect from the operation, but subsequently was affected with coryza. At the time of death, eighteen days later, the wound was perfectly healed, and no subcutaneous false bursa was noted. The mucous membrane of the frontal sinuses was injected, swollen, and covered with mucus. The dura mater and pia-arachnoid were everywhere free from congestion and quite natural in aspect. No subdural pellicle was present. The piece of false membrane implanted was white in colour. Adhesions had formed in its neighbourhood, and the cortex opposite exhibited a very small area of softening.

The dura mater and pia-arachnoid appeared quite normal in microscopic characters. Their nuclei were not definitely swollen nor increased in number. There was no subdural pellicle. No dilated blood-vessels were seen, nor were any fibrin filaments found. The inner layer of the dura did not stain yellow by v. Gieson's method, and no pigment cells were seen.

Loeffler's and Gram's method failed to reveal the presence of micro-organisms in any of the sections.

Experiment 9.—Dog. Operative procedure as before. There was no blood observed beneath the dura at the time of operation. Sterilised membrane was inserted. The animal was affected with a dry eczematous condition, chiefly over the head and in the axillæ.

Complete recovery took place after the operation. Animal killed and then decapitated twenty-six days later. Wound completely healed, no sign of sepsis, no subcutaneous false bursa. Both frontal sinuses were congested, and contained clear, slightly reddish fluid. At the vertex the subdural space contained a thin layer of dark red blood, chiefly on the left side. At the base over the cerebrum, pons and medulla was a large collection of blood about half a millimetre thick; it was difficult to say whether this was situated in the subdural or the subarachnoid space, or in both. The blood was effused during decapitation. The remains of the membrane inserted were whitish-grey in colour, surrounded by adherent meninges.

On microscopical examination a thin layer of unaltered blood was found on the inner surface of the dura at the vertex. The dura, however, showed no tendency to yellow staining by v. Gieson's method. There appeared to be no increase of cells, though the nuclei of the dura and pia were somewhat swollen. No pigment cells were found. There were no dilated vessels, and no fibrin filaments were recognisable.

No bacteria were found in any of the sections.

Experiment 10.—Dog. Operative procedure as before. Scarcely any blood escaped beneath the dura at the time of operation. Sterilised membrane inserted.

The operation was unattended by any ill effect. The animal was killed at the end of nineteen days, when the wound was completely healed. No subcutaneous false bursa was present. The dura mater was slightly congested; no pellicle was seen on its inner surface, which was shiny in aspect. The pia-arachnoid was very slightly congested.

The dura mater presented no marked change. Its inner layer showed some tendency to stain yellow by v. Gieson's method. There was in places on its inner surface a thin deposit of blood, the red cells of which were very little altered in aspect. This was probably effused by the tearing of vessels passing between the dura and pia occurring at the time of removal of the brain. A very few free cells were seen on the inner surface of the dura, some of which contained blood pigment. The nuclei of the dura mater were not swollen. The pia-arachnoid was natural in aspect. No dilated vessels were seen and no fibrin filaments were recognisable. Basophile cells, from most of which the granules were being discharged, were generally present in the dura.

No micro-organisms were present.

Experiment 11.—Cat. Operative procedure as before. There was scarcely any blood beneath the dura at the time of the operation. Sterilised membrane inserted.

No ill effect from operation. Animal killed at the end of twenty-six days. Wound healed. No sign of sepsis. A small subcutaneous bursa was found beneath the line of incision. Mucous membrane of the frontal sinuses was congested. The dura mater over the cerebrum exhibited a reddish-brown pellicle on its inner surface on the side of implantation. Slight congestion of pia-arachnoid.

The nuclei of the inner surface of the dura and of the pia were swollen, and the latter may have undergone some increase in number. There was no yellow staining of the dura or pia by v. Gieson's method. In some places the subdural space exhibited a layer of opaque material not staining yellow and apparently containing a very few free cells. Pigment cells are very rarely seen where this amorphous material is present; a very few pigment cells are seen lying on the dura elsewhere. It is not easy to determine the nature of this thin layer lying between dura and pia; it cannot be recognised as made up of altered bloods, and does not retain the stain by Weigert's fibrin method. No new vessels are seen, nor are any fibrin filaments recognisable.

No micro-organisms were found in any of the sections stained by Gram's and Loeffler's methods.

Experiment 12.—Cat. Operative procedure as before. Hæmorrhage into the subdural space was intentionally produced at the time of operation. Sterilised membrane inserted.

The animal showed no ill effect after the operation, and was killed at the end of twenty-one days. The wound was then perfectly healed. The mucous membrane of the frontal sinuses was congested, but the sinuses themselves were free from fluid. The inner surface of the dura mater, as also the pia-arachnoid, was generally of a yellowish tint, especially over the tip and base of the frontal lobe on the side of operation (left) and about the great longitudinal fissure, but no subdural pellicle was recognisable. The remains of the membrane inserted were of a greyish-white colour, adherent to the surrounding tissues.

On microscopical examination the pia-arachnoid and inner layer of the dura mater were found to stain of a deep yellow colour by v. Gieson's method, but no layer of blood was found in the subdural space, the walls of which were in close apposition.

The nuclei of the dura and pia were not swollen, nor were they increased in number. No pigment cells were present, nor were any fibrin filaments recognisable. None of the vessels of the membranes were dilated.

The staining of the dura and pia, unattended by the presence of pigment cells, appears to indicate that the hæmoglobin of the blood effused at the time of the operation rapidly dissolved out of the red cells, so that no blood film was formed in the subdural space and no phagocytosis of red cells occurred.

No bacteria were recognisable in any of the sections.

Experiment 13.—Cat. Operative procedure as before. Hæmorrhage into the subdural space was intentionally produced at the time of operation, and was greater than in the preceding experiment. Sterilised membrane inserted.

The operation was not followed by any recognisable ill-effect. At the expiration of fourteen weeks the animal was killed. The wound had completely healed. The frontal sinuses were reddened, but were free from fluid. There was no subcutaneous false bursa. The inner surface of the dura mater was of a yellowish tint at the vertex over the cerebrum on the side (left) of operation, and to a less extent on the opposite side, while at the base the dura was unchanged in aspect. There was no recognisable subdural pellicle. The pia-arachnoid was free from congestion, but was also tinted yellow over the cerebrum. In the situation in which a portion of sterilised membrane had been implanted in the subdural space newly formed fibroid tissue was found, which caused adhesions of the neighbouring structures.

On microscopical examination it was found that, by v. Gieson's method, the inner layer of the dura mater, the pia-arachnoid, and in places the immediately adjacent portion of the molecular layer, stained of a deep yellow colour. The subdural space was quite empty. The nuclei of the dura and pia were generally of large size, but had not undergone any increase in number. There were no pigment cells. None of the blood-vessels were dilated, and no fibrin filaments were present.

Staining methods failed to reveal the presence of bacteria in any of the sections.

Experiment 14.—Cat. Operative procedure as before. There was very slight hæmorrhage beneath the dura at the time of operation. Sterilised membrane inserted.

No ill-effect after operation was noted. Animal killed at the end of eighteen days. Wound completely healed. There was a small blood-stained bursa at the site of operation. The dura mater was free from congestion and unaltered in aspect. No pellicle could be recognised on its inner surface. The pia-arachnoid was slightly congested. The débris of false membrane implanted was found to be situated in the outer part of the cortex, which was softened all round. The dura and pia were adherent for a short distance at the site of implantation.

The inner layer of the dura mater was in places stained yellow by v. Gieson's method. The nuclei of the dura and pia were of large size, but were not increased in number. No free cells, pigment-holding or otherwise, were found in the subdural space. No dilated vessels were seen, nor were any fibrin filaments present.

No bacteria were present in the sections.

Experiment 15.—Cat. Operative procedure as before. No blood was seen beneath the dura at the time of operation. Sterilised membrane inserted.

No ill effect followed the operation. The animal was killed at the end of nineteen days. The wound was completely healed. The dura was free from congestion, and was unaltered in aspect except for slight roughness at the base. No subdural pellicle. Pia-arachnoid slightly congested. The remains of the false membrane inserted were of a yellowish-brown colour, attached to the inner surface of the dura, which was not adherent to the pia to any extent at the site of implantation.

No change was noted in the meninges outside the operation area on microscopical examination. There was no pellicle in the subdural space. No free cells, dilated vessels or fibrin filaments were recognisable.

No micro-organisms could be demonstrated by staining methods.

Experiment 16.—Cat. Operative procedure as before. Scarcely any blood was seen beneath the dura at the time of operation. Sterilised membrane inserted.

Operation was not followed by any ill effect. The animal was killed at the end of twenty-six days. The wound had completely healed. No sign of sepsis. There was no subcutaneous bursa, but the tissues in the area of operation were still blood-stained. The right frontal sinus was congested and contained bloody fluid; the left frontal sinus was congested but was free from fluid. The dura mater was unaltered in aspect, and presented no pellicle on its inner surface. Pia-arachnoid slightly congested. The dura was adherent to the pia at the site of implantation.

The inner surface of the dura was in some situations stained yellow by v. Gieson's method. The nuclei of its inner layer were not swollen. In one place a few red blood-cells were found lying on the outer surface of the dura. No subdural pellicle was found.

The nuclei of the pia-arachnoid did not appear to be increased in number. No pigment-cells were seen. Dilated vessels were not encountered, and fibrin filaments were absent.

No bacteria could be recognised by staining methods.

DESCRIPTION OF THE ILLUSTRATIONS.

FIG. 1.—Section of dura mater affected with internal hæmorrhagic pachymeningitis. The morbid process is advanced. Below is seen the dense fibrous tissue of the dura. The rest of the section is occupied by the newly-formed membrane, which is about a third of a millimetre thick, made up of delicate connective tissue strands arranged parallel to the surface, and covered externally with a layer of fibrin, the fibrils of which are readily recognisable. The laminated and œdematous character of the false membrane is obvious. There are numerous elongated, more or less flattened, darkly-stained nuclei to be seen, whose cytoplasm is not distinctly outlined. Besides these nuclei, others, which are less deeply stained and are sometimes smaller, and are surrounded by much cell-protoplasm, are seen lying upon the connective tissue strands, to which they are loosely adherent, being occasionally arranged side by side in a row. Five dilated blood-vessels are seen.

The fibrin on the surface exhibits a few nuclei. No extravasation of blood has occurred and no pigment cells are seen.

The flattened nuclei of the newly-formed layer are larger than those seen on the inner surface of the dense fibrous layer of the dura.

v. Gieson's stain. × 250.

FIG. 2.—Surface section of a recent grey œdematous subdural pellicle, not exhibiting extravasation of blood or cells containing blood pigment. At the lower part of the section is seen the inner layer of the dura mater, consisting of closely-packed connective tissue strands, the nuclei on the surface being large and numerous. The false membrane is made up of fibrin filaments, together with vessels of new formation and large size, though not fully distended. Free cells are also seen, especially near the dura. The outline of the cells is somewhat indistinct. Some granular material is also seen.

Weigert's fibrin stain. × 75.

FIG. 3.—The triangular area, bounded by blood-vessels, seen in fig. 4, more highly magnified. The individual fibrin filaments which are extravascular are more clearly seen, as is also the granular material accompanying, and in places closely adherent to, the filaments. Free cells with abundant granular protoplasm and irregular outline are seen sparsely scattered through the section. A few nuclei are also seen, mostly smaller and of darker colour, not surrounded by a recognisable ring of cytoplasm. The large oval flattened nuclei of the endothelium of the vessel wall are also seen. No pigment cells are present, and the blood-vessels do not contain any red blood-cells. A few filaments in the lower right hand corner are beaded. The shadows exhibited in the section are cast by portions of the section not in focus.

Weigert's fibrin stain. × 600.

FIG. 4.—Section of one of the dilated blood-vessels of the false membrane of hæmorrhagic internal pachymeningitis. A number of fibrin filaments, imperfectly stained and not occupying the whole of the lumen of the vessel, are present. Red blood-cells are seen and four white cells, two of which contain abundant cytoplasm, one exhibiting in addition blood pigment.

Stained by v. Gieson's method. × 550.

FIG. 5.—Section of dilated blood-vessel from the same membrane. A mass of fibrin filaments darkly stained is here seen, filling about a third of the interior of the vessel. The filaments are of a uniform structureless character, varying in thickness, and are cut across at right angles and in varying degrees of obliquity. In one place red blood-cells are seen lying between the fibrils; elsewhere the skein of fibrils is free from red cells. The rest of the lumen of the vessel is occupied by red cells, which are commencing to break up. Five hyaline cells are seen, four of which lie in clear spaces among the red blood cells.

Stained by Weigert's fibrin stain. × 550.

FIG. 6.—Section of a dilated vessel contained in the false membrane of Case 14. The lumen of the vessel is occupied by red blood-cells, among which lie filaments, some of large size, presenting an irregularly septate character. The surface stains more deeply than the rest of the filament, so that in transverse section a hollow appearance results. The smaller filaments stain uniformly or present an irregular granular character. In this case extravascular filaments, usually uniform, were met with in considerable numbers. Micro-organisms were also present, but are not seen in the figure.

Weigert's fibrin stain. × 700.

FIG. 7.—Section of a portion of the inner layer of the dura mater of Case 15, kept, together with the false membrane lying upon it, for five days on agar at 35° C. Between the collagen bundles, which are lightly tinted, a few filaments are seen stained. These do not appear to be contained in a blood-vessel. The largest filaments are deeply stained, the smaller ones are lighter in colour. The former do not exhibit divisions, but present irregular margins; the latter are septate, swollen in places, or even beaded, and stain more deeply at the periphery and along the septa than elsewhere. In contrast to the preceding figure the changes are more marked in the smaller than in the larger filaments. The section exhibits micro-organisms which, however, are absent from the portion sketched. A few nuclei are seen.

Weigert's fibrin stain. × 450.

FIG. 8.—Section of the inner layer of the dura mater of Experiment 10. The proper nuclei of the dura are elongated, lightly stained, and little if at all swollen. On the inner surface of the dura (to the left in the figure) new nuclei are apparent, of smaller size and less flattened than the former, and staining more deeply. In the cytoplasm surrounding some of the latter altered hæmoglobin (shown dark-coloured in the sketch) is seen in masses of varying size. No blood-vessels are recognisable, nor is any fibrin deposit seen.

Stained by Nissl's method. × 1,400.

FIG. 9.—The inner layer of the same dura mater seen from above. Only the surface nuclei, which are chiefly of new formation, are shown. Two kinds predominate, one large (but not so large as the elongated nuclei of the deeper layers of the dura) and lightly stained, the other small and darkly stained. The nuclei tend to be arranged in groups. Numerous dark pigment masses of very varying size are arranged about the larger nuclei. The outline of the cytoplasm of the cells is not seen owing to the absence of protoplasmic staining. No blood-vessels are recognisable, nor is any fibrin present.

Staining and magnification as above.

CASE OF TUBERCULAR TUMOUR OF THE SPINAL CORD IN A CHILD TWO YEARS OLD.

BY W. K. HUNTER, M.D., D.SC.,

Extra Physician to the Royal Hospital for Sick Children and Assistant-Physician to the Royal Infirmary, Glasgow.

THE following case is of interest not only as the record of a somewhat rare condition, namely, tubercular tumour of the cord, but also on account of some of the other morbid conditions which were found in the cord and medulla on microscopic examination.

Wm. D., aged two years, was first seen by me as an out-patient at the Children's Hospital on August 19, 1901. He was subsequently admitted into the wards under the care of Dr. Middleton, who has most kindly placed at my disposal his notes of the case, and to whom I am indebted for permission to publish it.

The history of the patient was briefly as follows. When six months old he had whooping cough, but excepting that he seemed to have been fairly well till he developed an attack of "pneumonia" at eleven months. On recovering from this he was "very weak," and made but little attempt to use his legs, though previous to the illness he could stand when holding on to a chair. Then, two months before admission, he had a second attack of "pneumonia," and on recovery his right arm was found quite powerless. Subsequent to this some paresis was also noted in the left arm.

At the time of admission to hospital he was a pale and rather ill-nourished child. The pupils were equal and reacted to light There was an internal strabismus of the right eye. The head was turned towards the left shoulder, and some rigidity was to be made out in the muscles of the left side of the neck. The right arm was completely paralysed and the muscles quite flaccid, but there was no apparent wasting of the muscle fibres: no tendon reflexes were obtained. The left arm still retained some voluntary movements, but there was a certain amount of rigidity, especially in the upper arm muscles. The arm was kept in the position of pronation, with the fingers closed on the palm of the hand, and on attempting supination the child evidently experienced a good deal of pain.

The right leg was extended, and there was a slight degree of rigidity in its muscles. No voluntary movement was to be noted. There was some slight movement to be seen in the left leg, but little or no rigidity. Both knee-jerks were exaggerated, the right more so than the left. Ankle-clonus was easily obtained in both. The plantar reflex was present in the left but absent in the right. The superficial reflexes all over the body were defective, and sensation as tested with a needle was evidently very defective, especially in the arms, but also in the trunk and legs.

There was no spinal deformity, and the organs of the chest and abdomen seemed quite normal.

The child's condition remained much as above described till about the middle of September, when unmistakable signs of meningitis developed. From this date onwards unconsciousness was more or less complete, and death supervened on September 29th. The temperature throughout ranged mostly between 100° and 101°, on very few occasions reaching 102°.

The *post-mortem* examination was made by Dr. A. R. Ferguson, to whom I am indebted for the following report, and by whose courtesy I have been permitted to investigate the microscopic appearances of the nervous system.

"*Head.*—The dura mater is slightly increased in thickness; it has no intimate connection with the bones of calvarium. The fontanelles are open. The surface of the brain is dry and glazed. There is considerable distension of the lateral ventricles with limpid fluid, and the entire ventricular system is proportionately dilated, the fifth ventricle also showing dilatation.

"There is a typical tubercular meningitis, distributed chiefly at the base and along the sylvian fissures. Tubercles are exceedingly numerous. There are no tubercular masses in any part of the brain.

"*Spinal Cord.*—The cervical enlargement is distinctly more voluminous than normal, and soft in consistency. The remainder of the cord presents no definite change on naked eye inspection. There is practically no fluid in the spinal meninges (*N.B.*—Lumbar puncture had been performed during life), and they are apparently free from inflammatory exudation.

"*Chest.*—The *heart* is atrophied. There is no degenerative change in the myocardium visible to the naked eye, and no lesion of the valves.

"The *right lung* is intimately adherent at the apex, and its removal is only effected by tearing, in which a tubercular cavity at the apex is opened into. This is subdivided into a number of intercommunicating loculi (none large), and some of which at least are of bronchiectatic origin. There are scattered tubercles throughout the remainder of the lung. The bronchial glands are enlarged and caseous. The *left lung* shows a lesser tubercular infection.

"The *spleen, kidneys* and *liver* are free from tubercles so far as this can be affirmed by naked eye scrutiny. The kidneys are anæmic and the liver fatty. The mucous membrane of the *stomach* is catarrhal. The *intestine* contains numerous tubercular ulcers of recent appearance. These are chiefly met with in the lower part of the ileum. The mesenteric glands are enlarged and partially caseous."

The pons, medulla, and cord were placed for twenty-four hours in 10 per cent. formol. After that certain segments were transferred to Müller's fluid, the rest being retained in formol solution so as to fix them for Nissl's stain. Sections from the former segments were stained by Marchi's and by Weigert's methods, and those from the other segments by theonin and by hæmatoxylin and eosin.

On more detailed examination of the cord the swelling in the cervical region mentioned in the above report was seen to occupy five segments (about one and a half inches in length), beginning at the second pair cervical nerves and ending at the seventh cervical. On transverse section the cause of this enlargement was found to be a tubercular nodule, somewhat oval in shape, about three-quarters of an inch in length, and occupying the centre of the cord, with but a narrow rim of cord tissue surrounding it. Its upper end occupied part of segment three, and the nodule extended through the whole of segment four and the greater part of segment five. Its greatest breadth was in segment four, where it measured transversely half an inch. The general outlines of the tumour in transverse section are shown in the diagrams. All the figures from the cord are drawn by the aid of the camera lucida, and they represent more or less accurately the proportion in size of one transverse section to another and to the various elements which each contains. The first indication of the tumour is in figure C_2, which is from the lower end of the second cervical segment, or possibly from the upper part of the third cervical. This section lies adjacent to the upper end of the tumour, and the deformity of the gray matter on the right side of the section was doubtless due to pressure of the tumour, the upper end of which occupied, most probably, the foramen indicated in that part of the section. The figures C_3, C_3', C_4, and C_5 all show succeeding levels of the tumour. As far as can be made out, the growth has commenced in the right posterior horn, which has to a large extent been obliterated. The right anterior horn has also almost entirely been destroyed. It is quite lost in C_4, but it is represented in C_3' and C_5 by a few ganglion cells lying immediately along the right margin of the tumour. The left anterior and posterior horns are uninvolved throughout.

As to the ganglion cells in this gray matter, it is astonishing how little alteration they really have undergone. In sections at the upper end of the tumour (C_3) the majority of the cells in the right anterior horn certainly show chromatolysis, *i.e.*, fragmentation of the Nissl-granules; but the nucleus in most still remains central and the cells still retain their processes. Even the ganglion cells at the margin of the tumour, and which are being surrounded by inflammatory cells, show but little change beyond some fragmentation of the granules. In the left anterior horn there is also a fair proportion of cells showing commencing chromatolysis, but not so many as in the right horn. At levels C_3' and C_5 the ganglion cells of this left anterior horn show practically the same appearances as in C_3; and a count of the number of cells in this left horn at these different levels confirms the impression that very few cells have disappeared as a result of the chromatolytic process. Only four or five cells are to be seen in the remnants of the right anterior horn in C_8' and C_5, but most of these, though undergoing degenerative change, still retain their nucleus.

The tumour itself is certainly tubercular. Its centre has undergone caseation, and is surrounded by a dense but somewhat narrow ring of cell formation. The most dense parts of the ring surround blood-vessels, and here round cells are most abundant. In other parts of the "ring" the round cells are mixed up with spindle-shaped cells and epithelioid cells. Here and there, round the margin of the tumour, groups of cells are seen extending out a short distance into the gray and white matter of the cord, and inwards into the caseating centre.

The white matter surrounding the tumour is best studied in the Marchi sections (C_4), but even here it is difficult to be quite certain of its identity. It is clear, however, that the pyramidal fibres remain intact, for no degeneration is found in the motor tracts at the eighth cervical, or in any of the other Marchi sections lower down the cord. Judging, however, from the section C_4, one would have looked for degeneration in the right pyramidal tract, which at this level must be greatly flattened out, and in close association with many degenerate fibres from other tracts. Both direct cerebellar tracts show degeneration, especially the right. Only the left posterior column remains, and its fibres have also undergone degeneration. The right posterior column cannot be recognised, and it doubtless has been displaced by the tumour. The left antero-lateral tracts contain some scattered degenerate fibres, but the right antero-lateral tracts are not clearly to be made out.

The degenerated fibres above and below the tumour are indicated in the diagrams. From these it will be seen that there is a marked degeneration at the eighth cervical segment (C_8) in the posterior columns, being more intense in the postero-external than in the postero-internal tracts. It is to be noted, too, that in the right postero-lateral tract there is a wedge-shaped area giving no reaction with the Marchi stain, but showing with Weigert's method a degeneration of older standing than is to be seen in the other fibres at this level. Both direct cerebellar tracts also contain degenerate fibres, and there are some few degenerate fibres scattered through the antero-lateral tracts.

Passing down the cord (T_1, L_1, L_4, and S_1) the sections are seen to be almost free from degenerate fibres, and where these do exist they are not closely grouped into any definite tract. In most of the sections there are a certain number of blackened fibres round the margin of the cord; the rest are mostly scattered through the posterior columns.

Above the tumour (C_8 and C_1) the degeneration of the posterior columns is still marked, being most intense in the postero-lateral tracts, and still showing the wedge of more advanced degeneration on the right side, the same as seen in C_8. In the two sections of the medulla the degenerate fibres are found surrounding the nucleus gracilis and nucleus cuneatus, and they can be traced passing forwards in the internal arcuate fibres and upwards in the fillet of the upper medulla. In the section of the pons (level of seventh nerve), the degenerate fibres of the fillet are not very certainly made out. Neither are the degenerate fibres of the direct cerebellar tract to be seen at this level, though they are well shown in the sections of the medulla.

As regards the ganglion cells of the gray matter above and below the tumour, there is not very much to say. At the sixth cervical segment (C_6) of the ganglion cells in the anterior horn, those in the antero-lateral groups are fairly healthy. But in the left postero-lateral group about 50 per cent. are seen to be in different stages of a commencing chromatolysis. This seems to be a central chromatolysis, *i.e.*, it commences round the nucleus and progresses towards the periphery of the cell. The right postero-lateral group shows a smaller proportion of these degenerate cells, but on counting the number of cells in this group there are found to be only about half as many cells as in the left postero-lateral group; the number in this left postero-lateral group may be taken as normal.

On passing into the seventh cervical segment the degenerative changes are much more marked, for throughout the whole of this segment (sections were examined at three different levels) scarce a single normal cell is to be seen. The vast majority of cells have a homogeneous plasma without any granules whatever. A few have some peripheral granulation. Most have a peripheral nucleus; but in a considerable proportion the nucleus has entirely disappeared. The different groups of cells seem to be equally affected, and on a count being made practically no diminution in the number of cells can be found. All the sections in this seventh segment show a great invasion of inflammatory cells. This is specially marked, passing in with the posterior roots, and throughout the gray matter.

Throughout the whole of the dorsal region of the cord (eight levels were examined) the ganglion cells were found quite healthy, and this applies also to the cells of Clarke's column. The same may likewise be said of the lumbar and sacral regions.

Sections were also examined from the upper part of the first cervical segment, and here the appearances were very similar to those described in the sixth cervical, *i.e.*, about half the ganglion cells show an early degeneration.

The only two motor nuclei which appear in the Nissl sections of the brain are the seventh and twelfth, and the ganglion cells in both of these are practically normal.

As to the meningitis referred to in the *post-mortem* report, this is well seen in the sections stained with hæmatoxylin and eosin. It is most intense in the pons and medulla, for here the pia is densely infiltrated with cells, the infiltration being most marked round the vessels. The majority of the cells are round cells (leucocytes), but there are also a considerable number of epithelioid and spindle-shaped cells. Also, and especially in groups, there are some larger, round cells with deep-staining central nucleus, which have been called "contractile cells." A few giant cells are likewise made out. There is no caseation in any of the nodule-like collections of cells. A certain amount of infiltration of these inflammatory cells into the substance of the pons and medulla is also to be seen. This is most marked in the neighbourhood of the fourth ventricle, but there is also a slight increase of the connective tissue cell element throughout the whole section, though except at certain parts of the periphery it is by no means well marked. This infiltration should doubtless be regarded as an exudation from the vessels rather than an increase of the neuroglia cells, but that there is no increase of these cells it is difficult to be certain.

The pial investment of the cord shows the same cellular infiltration as that of the medulla, though it lessens much in intensity in the dorsal, lumbar and sacral regions. It always seems to be most intense round the posterior roots, and at this point, in some of the sections, there is quite an invasion of inflammatory cells into the substance of the cord. This is very marked in the seventh cervical segment, where the infiltration into the posterior columns and gray matter of the cord is most striking: it is doubtless the cause of the degeneration of the ganglion cells already described as being present at this level. This same infiltration, but to a much less extent, is seen in the sixth cervical segment, and to a still less degree in the dorsal, lumbar and sacral regions. In the antero-lateral tracts at these last-mentioned levels there is practically no increase of the connective tissue elements.

The central canal throughout the whole extent of the cord shows a slight amount of dilatation.

It has just been said that in the section of the cord the meningitis seemed most intense round the posterior roots. It is also to be noted that in all the sections from the cervical region the posterior roots, as they lie within the cord, give a well-marked reaction with Marchi's stain. But in striking contrast is the appearance of the roots before entering, *i.e.*, as they lie outside the cord, for in very few of the sections do these roots show any blackened fibres whatever. For example, in C_1 and C_8 the posterior root external to the cord gives no degenerative reaction, but the moment the boundary of the cord is crossed the degeneration of the fibres becomes very marked. In C_2 and C_4 the right posterior root gives a slight reaction where it is outside, but the reaction is nothing like so intense as when the fibres have entered the cord. In the dorsal, lumbar, and sacral regions the root within the cord gives a slight reaction, and this only at certain levels; but external to the cord there is practically no blackening of the fibres whatever.

Of peripheral nerves, the right vagus, the right median and right posterior tibial were all examined, but none gave any reaction with the Marchi stain. It is to be noted, however, that these same nerves, when stained with hæmatoxylin, showed an undoubted increase of the internodal nuclei, which, I take it, indicates an early degenerative process going on in these nerve fibres, though the myelin has not yet become fatty.

That, then, is the case as it presented itself to us; and in considering it in the light of the above report it is evident that there are two quite separate morbid conditions to be considered, namely, the tubercular tumour and the tubercular meningitis. Of the tumour little requires to be said beyond mentioning that such tubercular nodules of the cord, unassociated with tubercular nodules in other parts of the nervous system, are very rare, or, at least, very few such cases have been put on record.

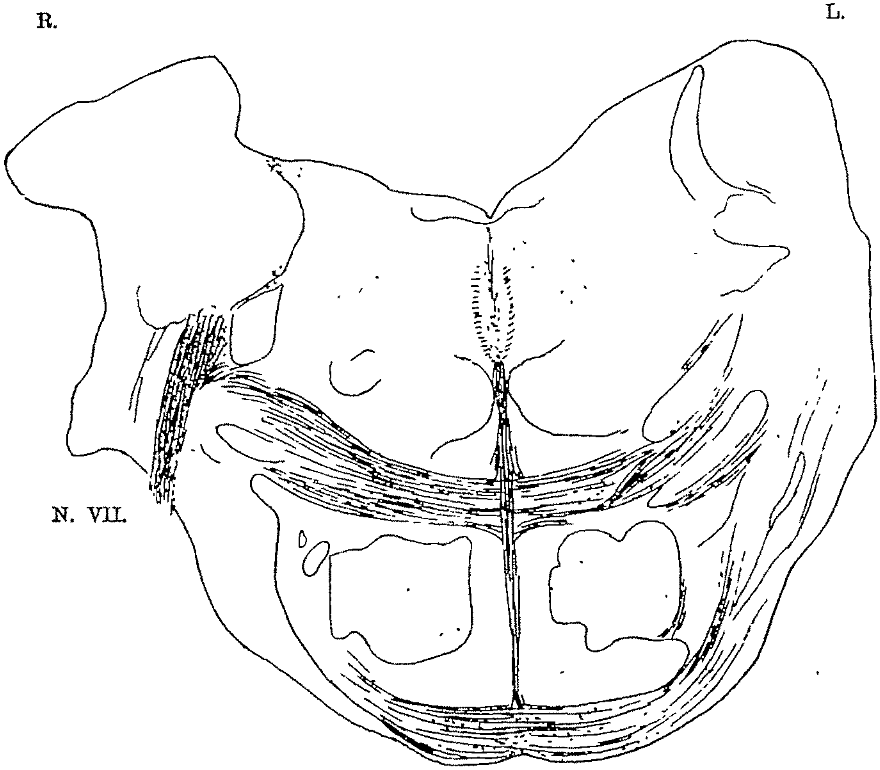
As to the degenerations above and below the tumour, these must be looked on as due rather to the meningitis than to the tumour itself. The proof of this lies in the fact that the ascending degeneration is quite as marked in the eighth cervical as in the second cervical segment; also it may be added that there is no degeneration of the pyramidal tracts below the level of the tumour.

The meningitis may, then, be taken as the chief cause of the ascending degenerations; and it would seem to produce its effect in two ways: first, by acting directly on the ascending fibres themselves, and, second, indirectly by its effect on the posterior roots. That the degeneration in the posterior columns is due mainly to involvement of the posterior roots is evident on looking at sections C_8, C_2, and C_1. In these the fibres in the postero-lateral tract (root zone) are chiefly affected, and their distribution is much the same as that which has been produced experimentally by section of a posterior root at this level. But the degenerate fibres in the postero-median tract (column of Goll) in, for example, C_8, cannot be explained in this way; for we know that none of the fibres in the column of Goll, in the lower cervical segments, enter the cord by roots higher than the mid-dorsal region, and that they probably enter by roots a good deal lower down. Now, in the sections below the mid-dorsal level in our case there is no sufficiently marked degeneration of posterior roots or root zones to give such a well-marked degeneration as is found in the postero-median tract at C_8; so that I am disposed to attribute the most of the degeneration in this tract, at least in the lower cervical segments, to the direct action of the meningitis, either from the pressure of its exudation or from the poisonous action of the toxins which this exudation contains. The degeneration of the direct cerebellar tracts must also be explained in this way, for they show no degeneration in the dorsal region, neither is there evidence of involvement of the cells in the columns of Clarke. And if the direct cerebellar tracts may be affected by the meningeal exudation, there seems no reason why the columns of Goll, at least their most superficial parts, should not be affected also.

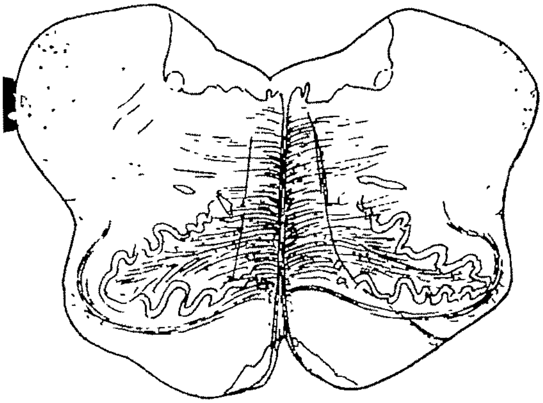
The degeneration of the posterior roots is probably also due to the direct action of the exudation, which would seem to penetrate more readily to the part of the root within the cord than to the part which lies without, and which is still invested with its sheath. This will perhaps explain why the degeneration is so much more intense in the part of the root within than in that lying outside of the cord.

The "comma" tract of Schultze shows no evidence of degeneration in any of the sections from the upper dorsal region. This is a matter for comment, for in the fourth cervical segment there seems to be a total loss of the right posterior column, and as a result one would look for a descending degeneration in the "comma" tract on this right side.

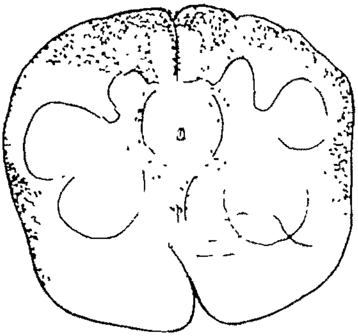
Of the degenerate fibres which pass up in the posterior columns to the medulla, we have seen that this degeneration



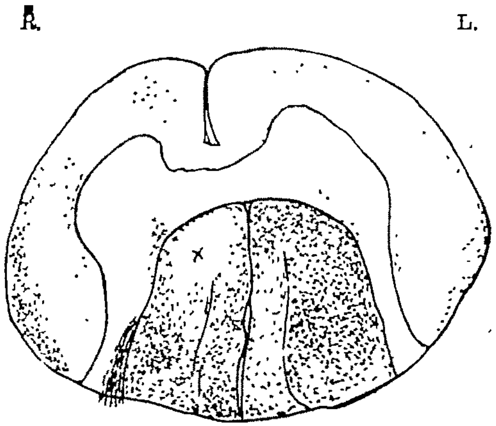
Pons.



Upper Medulla.

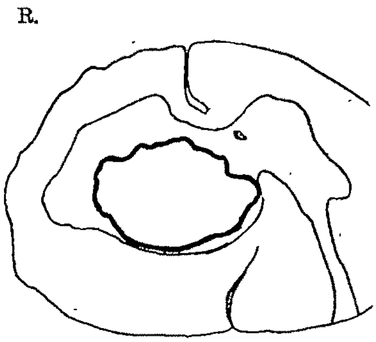


Medulla.

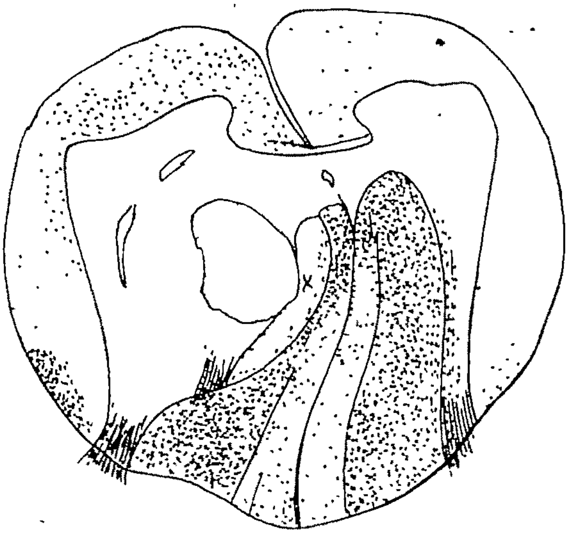


C_1 (Marchi).

X—This area shows degeneration with Weigert's stain.

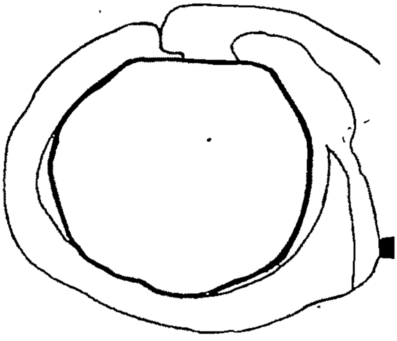


C_3 (Nissl).

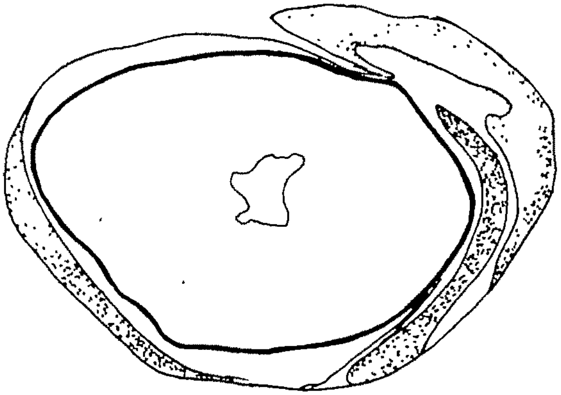


C_2 (Marchi).

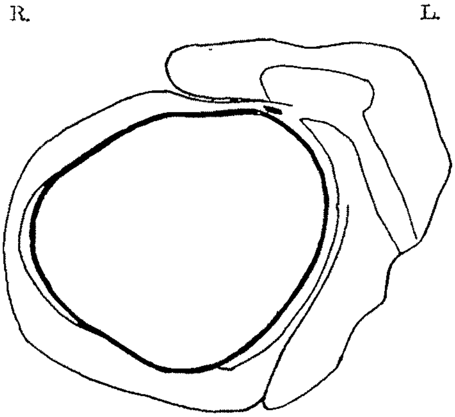
X—This area shows degeneration with Weigert's stain.



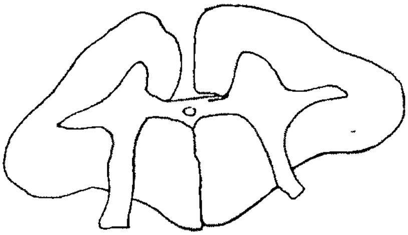
C_3' (Nissl).



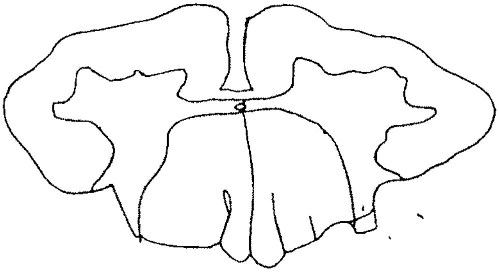
C_4 (Marchi).



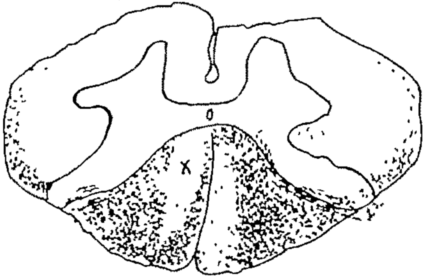
C_5 (Nissl).



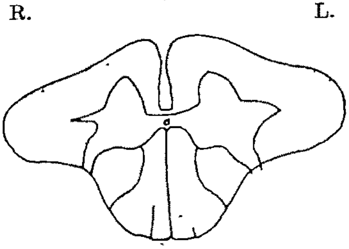
C_6 (Nissl).



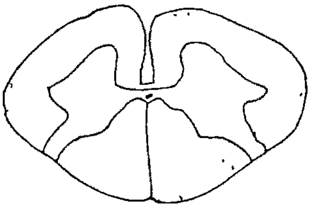
C_7 (Nissl).



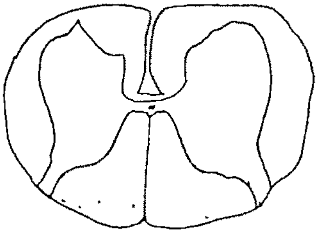
C_8 (Marchi).
X—This area shows degeneration with Weigert's stain.



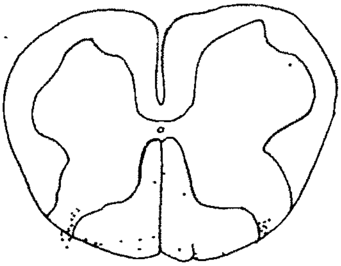
T_1 (Marchi).



L_1 (Marchi).



L_1 (Marchi).



S_1 (Marchi).

A CONTRIBUTION TO THE PATHOLOGY OF ACUTE INSANITY.[1]

BY DAVID ORR, M.B.

Pathologist to the County Asylum, Prestwich, Lancs.

To those who are daily brought in contact with the insane the subject of the acute forms of insanity must always be of interest, not only on account of the varied clinical pictures which cases of acute mental disorder afford, but also on account of the variety of ways in which such cases may terminate.

But the class of case which must be of the greatest interest to the alienist is that which unfortunately tends towards a fatal issue in spite of all that medical science can do; and it is only too often that those who have charge of our asylums have to record such cases as dying from "exhaustion."

Even in such a limited experience as the writer's, cases of this nature have occurred not infrequently, and one must be struck by the fact that to a naked-eye examination of the organs of such cases there is often nothing to account for a fatal termination.

It was therefore with the view of ascertaining the morbid changes found in the central nervous system of these cases that this study was undertaken, in the hope that a knowledge of the pathological anatomy might direct one's steps towards a further and future investigation into the factors which bring about these grave alterations of mental function. It was decided, therefore, to examine microscopically the nerve cells and conducting fibres of the central nervous system of six cases of acute insanity, always taking the precaution that these cases were of recent origin, and the writer has endeavoured to employ the most recent methods of research in order to eliminate as far as possible any appearance which might be construed as due to faulty technique.

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[1] Submitted for the Degree of M.D., Edin.

It often happens that material from a case of interest from the pathologist's standpoint is rendered unsuitable for research on account of *post-mortem* changes.

In the present series one has had the good fortune to avoid this, so that before commencing a description of the morbid appearances found, one can definitely affirm that the changes detailed below are not complicated by the presence of putrefactive changes in the tissues previous to fixation and hardening.

Case 1.—S. D., aged 52, a widow.

HISTORY PREVIOUS TO ADMISSION INTO THE ASYLUM.

She has always been known in the neighbourhood in which she resided to be a hard-working woman of steady habits. A few weeks before the onset of her mental failure she complained of not being able to sleep, and it was noticed that she rambled somewhat in conversation and that she talked to herself a good deal.

Her symptoms progressed, until one week before admission she was so irrational in conduct and so noisy that her removal to the workhouse became necessary. While there it was noted:—She was violent, noisy, incoherent, restless and destructive, running round and round the room and tearing her bedding to pieces. She remained there four days, and was admitted to Prestwich Asylum on February 1, 1901.

STATE ON ADMISSION.

Physical Condition.—She is a tall, dark, thin woman; rather emaciated. Lungs apparently healthy. First sound of heart rather muffled and faint. Her reflexes could not be examined on account of her extreme restlessness and violence.

Mental State.—She is very excited and restless, wandering round her room continually, talking in a rambling and incoherent manner. Her attention cannot be arrested, and she does not answer questions put to her. She is destructive and dirty in habits. During the next few days she remained in much the same mental state—excited, noisy, refused food, and was out of bed all night. On February 5 she was noticed to be becoming weaker on account of her extreme restlessness, and on February 6 her temperature was found to be 102° in the evening. This was ascertained with great difficulty, owing to her constant struggling.

On February 7 the restlessness and excitement were unabated, and she died suddenly at 10.30 a.m. on February 8. Only on one occasion could the temperature be taken.

AT THE AUTOPSY.

There was very little of a pathological nature visible to the naked eye.

Both lungs were œdematous, and in the right lung at the base there was a considerable degree of congestion. The heart muscle, to naked-eye examination, appeared to be normal. In the kidneys the capsule was found to be slightly adherent.

In the brain nothing was apparent to naked-eye examination beyond a distinctly patchy pink colouring of the grey matter seen on slicing into the brain. The following tissues were preserved for microscopic examination:—Tissue from the fronto-motor region of the left half of the brain; slices from the cervical and lumbar enlargements of the cord for nerve-cell examination, the remainder of the cord being preserved for the examination of the sheaths and axis cylinders; posterior root ganglia from cervical and dorsal regions.

The methods employed for the examination of the nerve-cells and fibres were identically the same in all the six cases to be described, so any details need only be given in the description of Case 1.

Cortex.

Fronto-motor-region.—In order to study the appearances in the nerve-cells, the tissue selected was treated by Heidenhain's corrosive sublimate method, and subsequently stained with toluidin blue and by Robertson's methyl violet method. The tissue to be stained with toluidin blue was embedded and cut in paraffin; for Robertson's method the tissue was embedded in dextrine and cut by Swift's ether-freezing microtome.

The following appearances are noted:—The giant cells and large pyramidal cells show the smallest degree of affection of the chromophile or Nissl bodies. At first sight one might think that many of those cells were normal, but the change, although slight, is revealed by high powers. One can see that the chromophile elements throughout the cell show a distinct rounding of their outlines, and between the individual elements there is a deep, diffusely-stained substance which tends to obscure and render indistinct the outline of the Nissl bodies. The nucleus also stains diffusely, but the nucleolus stands out very sharply. This is the earliest morbid change noticeable.

While some cells may show this change, others present a distinct chromatolysis around the nucleus, the chromophile substance being here reduced to a fine powdery dust, while towards the external zones of the cell the normal blocks of chromophile substance are abundantly present. In a considerable number of cells the chromatolysis is found more advanced at the base than in the perinuclear region, and one finds it difficult to determine whether the disintegrative process is primarily basal or perinuclear.

But even where the disintegrative process does commence at the base of the cell, a rapid extension to the perinuclear region quickly follows. In the chromatolysed area minute granules of fragmented chromophile substance are found lying amidst a deeply-stained fundamental groundwork.

The protoplasmic processes are as a general rule rather paler than usual, and seem to be more deficient in chromophile substance the farther out one passes from the cell body. The nucleus almost constantly retains its central position, displacement towards the periphery of the cell being very infrequent.

In the medium-sized pyramidal cells one constantly finds chromatolysis, which, however, does not affect all the cells to the same degree.

In a few cells there is a slight fragmentary change which affects all the Nissl bodies generally throughout the cell, small pieces of chromophile substance being detached from the edges of those bodies and lying free in the fundamental amorphous substance. One region of the cell is not affected more than another.

The great majority of cells present a more advanced stage of disintegration, the type of chromatolysis being distinctly of the central or perinuclear variety. Here the space around the nucleus is quite denuded of chromophile material, and round the periphery of the cell only a band of chromophile substance is left, the elements of which are themselves affected by the fragmentary change, their outlines staining somewhat indistinctly and showing great irregularity. A more advanced stage of degeneration is met with, in which there is pallor of the nucleus, and the cell-body with its processes is reduced to a pale, diffusely-staining protoplasmic mass.

In studying the small pyramidal cells one is struck by the fact that their nuclei have a great affinity for the aniline stains, especially for the methyl violet. These nuclei colour very deeply and diffusely, so that the nuclear network is totally obscured, and in many cases the nucleolus is recognised with great difficulty.

The cell protoplasm stains very faintly, especially in the vicinity of the nucleus; and at the periphery of the cell, where the colour is deeper, slight traces of granularity are to be observed, and must be regarded as Nissl bodies in the last stage of dissolution.

Spinal Cord.

Cervical Enlargement.—Two thin slices were taken from this region and placed in a mixture containing equal parts of saturated corrosive sublimate and saturated solution of picric acid for twenty-four hours.

The pieces of tissue selected were hardened in spirit and embedded by the combined paraffin and celloidin method. The sections were stained with toluidin blue.

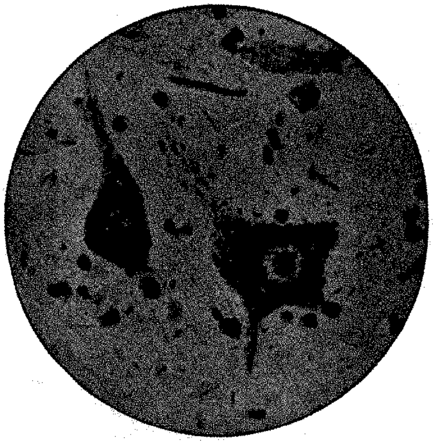
Among the large cells of the anterior horns a few show a slight degree of morbid change. The chromophile substance seems to be rather smaller in quantity than normal, and there is an increase in the interval between the individual elements. In addition, the shape of the elements is slightly changed, their edges being smoother and rounder, as if some of the chromophile material had been lost. It is evident that those cells show little departure from the normal appearance.

There are numerous cells in which a perinuclear chromatolysis is evident. This, as a rule, is limited strictly to the region immediately surrounding the nucleus, and here the chromophile material is greatly fragmented, appearing as a fine dust.

At the periphery of the cell and in the protoplasmic processes, the chromophile substance is normal in shape and quantity, while the nucleus retains its central position and stains well. Very occasionally in the large cells one finds a dissolution of the entire chromophile substance; very fine granules are alone left, and the cell body stains in an intensely blue manner throughout. Here the nucleus assumes an excentric position.

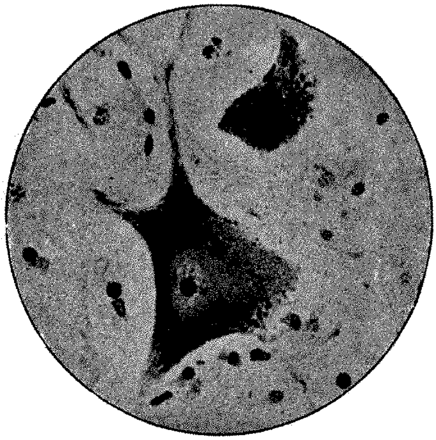
In the smallest cells of both anterior and posterior horns the chromatolysis is much more advanced; some show little or no chromophile substance, and they stain diffusely and weakly with the aniline dye. Here and there cells showing an increase of pigment in the cell-body are found.

Lumbar Enlargement.—The pieces of tissue taken from this



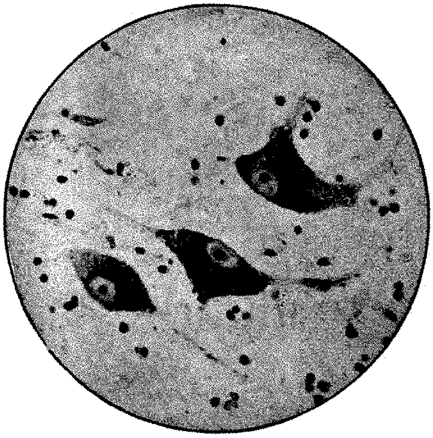
Photograph 1.

Note the slight degree of chromatolysis affecting one side of the larger cell.
Spinal cord.



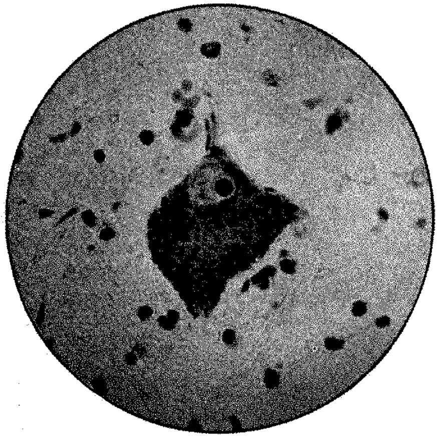
Photograph 2.

Note how the process of chromatolysis has affected one side of the cell, and is spreading round the nucleus.
Spinal cord.



Photograph 3.

Three cells showing central chromatolysis, with excentric nucleus.
Spinal cord.



Photograph 4.

Note the peripheral situation of the nucleus. The chromophile elements are much fragmented and stain faintly.
Spinal cord.

region of the cord were fixed, embedded, and stained precisely in the same manner as those taken from the cervical region. The types of morbid change found in the nerve-cells are the same as those already described above, but in this situation some cells show a more profound degree of chromatolysis. The area around the nucleus, in which the chromophile elements are fragmented, is much larger than in any of the cells of the cervical enlargement, and the nucleus tends to assume an excentric or peripheral position (Photograph 3). Again, one notices, rarely, cells of a pale diffusely blue appearance in which there is complete dissolution of the chromophile elements and pallor of the nucleus, which is excentric. Sometimes in those cells the central portion of the cell-body stains more deeply than the peripheric portions.

Posterior Spinal Root Ganglia.

The fixation, hardening and embedding of these structures have been the same as in the case of the spinal cord, and the combined celloidin and paraffin embedding method has been of special value for the study of the delicate cells in those ganglia.

The cells of the posterior root ganglia are affected to a very considerable extent by chromolytic change; the form the degeneration assumes, however, is very different in appearance from that observed in the cervical and lumbar enlargements of the cord. The reason for this is evident when one considers that the cells here do not possess normally uniform characteristics, some of them having very delicate granuliform chromophile elements, while others have their chromophile material in the form of large definitely-shaped blocks as in the cells of the anterior cornua of the cord and in the cerebral cortex. The different types of cell normally met with in the posterior root ganglia have been fully described by Lugaro (16), and in a paper by the author written in collaboration with Dr. Rows (26), but it will be sufficient here to direct attention to two of the chief cell types, the recognition of which will help the reader to understand the morbid appearances to be described.

The first form of cell which interests us, on account of the frequency with which one finds it affected in the acute insanities, is the large type in which the chromophile elements are small and granuliform, both around the nucleus and in the central parts of the cell generally. Towards the edge the chromophile granules may either be found of a slightly larger size, or there may be a distinct single row of large, slender, elongated chromophile elements extending completely round the periphery of the cell.

Elsewhere the chromophile granules are exceedingly small and densely crowded together. One other point worthy of notice is that the nucleus is central, and around it there is a clear narrow ring, quite free from chromophile material, called the perinuclear space.

The second type of cell is that of medium size, in which the chromophile granules are much fewer in number but of larger size than in the above type. Here again the nucleus is central.

The degree of chromatolysis varies considerably in both the first and second cell types. In the cells containing small granuliform chromophile elements one finds these elements breaking up in the centre of the cell into still smaller fragments, losing their affinity for the stain and disappearing, until a condition of complete achromatosis results. The nucleus usually retains its central position, but may be excentric in some cases.

When a cell has become so degenerated as to lose its entire chromophile substance, it stains in a faint diffusely blue manner, but still retains its normal outline. But in many a further degenerative stage is shown by an increasing pallor and atrophy of the nucleus, which becomes reduced to a pale, diffuse, and shadowy structure in which no details are discernible. At this stage the cell—which may be safely assumed to be dead—is seen very often to be invaded by large oval or round nuclei.

In some of the large cells the amount of morbid change found in the chromophile elements is not great, being confined to a slight loss of their affinity for the stain and a slight reduction in their numbers. But here one frequently finds a definite degeneration of the nucleus, which stains deeply and diffusely blue in such a manner as to obscure the nuclear network entirely and the nucleolus partially. At the same time an atrophic process accompanies the alteration in staining reaction, so that a nucleus may be reduced by one-third of its original size, giving rise to a great increase of width of the perinuclear space. It would seem in those cases as if the nucleus had been less able to resist the tendency to degeneration than the chromophile elements in the cell-body.

In the cells possessing large chromophile elements normally, the chromatolysis can be shown to be a central one. The elements break down, in the central parts of the cell, into fine, minute, dust-like granules. The nucleus passes rapidly to the periphery of the cell, where the least degenerated elements persist, forming a ring round the cell margin, being especially dense in the neighbourhood of the nucleus itself.

In addition to the process of chromatolysis described above, vacuolar change may be present in the cells of the spinal root ganglia. In the large cells with minute chromophile granules a clear space may be present, occupying at times one-third of the entire cell-body, in which there may or may not be seen any detail of cell structure. When any structure is apparent in those spaces it is usually of a fibrillar nature. These vacuoles—if one is justified in calling them so—are entirely surrounded by chromophile elements, and more than one may be present in a cell whose chromophile elements show little or nothing of disintegrative change.

An opinion as to whether such a form of vacuolation can be taken as evidence of morbid change must be given with great reserve on account of the fact that it has been my experience to find exactly similar appearances in the posterior root ganglion cells of presumably normal dogs, rabbits, cats, and hedgehogs.

Vacuolation of quite a different type is met with in those cells already referred to as being in a condition of achromatosis with degenerated nucleus, and which one regards as dead. In the faintly blue stained protoplasm which is left, round or oval vacuoles are present, varying in number from one to five or six.

Medullated Fibres of the Spinal Cord.

In transverse sections of the spinal cord, stained by the *Wolters-Kulschitzky* modification of Weigert's method, the colouring of the crossed pyramidal and postero-internal columns appears lighter if the specimen is examined with the naked eye. Under the microscope many of the nerve-tubes stain feebly, and are thinner than normal.

To study the degenerations of the myelin sheath I have used a modification of Marchi's method published by me some time ago (25).

The mixture into which the tissues are placed differs from that of the original Marchi method practically only in the addition of one part of acetic acid, 1 per cent., to 4 parts of osmic acid, which is used in 2 per cent. solution.

Formerly bichromate of potash was omitted, but now I always add this to the osmic and acetic acids.

Pieces of tissue thus treated for ten days should be washed overnight in running water.

The addition of acetic acid favours penetration very considerably, and for two years my results have been invariably constant, and up to the present time the sections are permanent.

In transverse sections of the cord so treated one sees a small number of black dots—indicating degenerated fibres—scattered about all over the cord. These degenerated fibres are found in all the tracts, but in some tracts they are more numerous than in others. In the anterior and antero-lateral columns only a few are seen. In the crossed pyramidal and posterior columns they are more numerous. The degeneration in the crossed pyramidal tracts is equal on both sides; in the posterior columns slightly more degeneration is present in the postero-internal.

A considerable number of black degenerated myelin droplets are met occasionally in Lissauer's tract and in the posterior horns. In the above-noted columns the degeneration has not the character of that found in descending or ascending system lesions, for the affected fibres are separated from each other by considerable numbers of fibres which yield no reaction, so that the degeneration assumes a diffuse, scattered character.

In longitudinal sections the degree and nature of the myelin sheath and axis cylinder changes can be much better studied. By the Marchi method, looked at with a low power, one recognises the typical rows of black droplets indicating myelin degeneration. These rows do not exceed more than three or four in one field. Sometimes the rows are of considerable length; others, again, are much smaller. There are many black droplets scattered throughout the section.

A *combination of the Marchi method and safranin staining* has been found exceedingly useful. Sections from tissue prepared by Marchi's method are transferred without any further treatment into a dark red watery solution of safranin No. 0, and stained overnight. They are then washed in methylated spirit until the stain ceases to come out, transferred to absolute alcohol, cleared in xylol, and mounted in Canada balsam.

Adamkiewicz recommends washing in alcohol acidulated with nitric acid, and then differentiation in clove oil. This has been discarded, as the bleaching action is at times too great.

By this combination the finer myelin changes are brought out, and the contrast between the Marchi degeneration and the myelin atrophy and absorption, to be described, is very well demonstrated.

There are a few myelin sheaths in which there are no changes visible.

In those which are morbid, some parts of the myelin tube stain well with the safranin, assuming a rich pink colour, and inside the axis cylinder is visible. On both proximal and distal sides of this well-coloured segment of sheath one finds other portions in which the staining reaction is much less, and instead of being pink is a light violet tint. Here there is dilatation and thinning, and at irregular intervals there are small clear vacuoles. In those thinned segments, which indicate an atrophic process, the axis cylinder also stains a light violet colour.

In the medullated fibres there are occasionally seen definite constrictions exactly like nodes of Ranvier, and on either one or other side of the constriction the myelin sheath may show the atrophic process very distinctly.

Many of the sheaths possess a beaded appearance, small collections of pink-stained myelin lying around the axis cylinder at intervals, while between the beads the myelin forms a very thin coating. The axis cylinder runs usually along one side of these dilatations, rarely through their centre, and in this situation may be very varicose.

At some points in the course of the nerve the myelin becomes broken up into lightly violet staining droplets or masses, and amongst these the axis cylinder lies faintly stained, and in many instances thinner than normal. The atrophy of the sheath may be complete at certain parts, leaving the axis cyclinder completely denuded.

Very occasionally one sees rupture of this latter structure, the severed ends terminating in a swollen, curled-up bulb.

In this case, and also in the others, longitudinal sections were stained by Wolter's method, but the results were such as to lead one to discontinue its use, and rely solely upon the combined Marchi and safranin method.

Case 2.—A. C., aged 48, married.

History Previous to Admission into the Asylum.

Twenty-one days before her admission to the asylum the patient was confined, giving birth to a living full-time child. Parturition was not accompanied by any accident or complication, and all went well until one week after the event, when one of her children died suddenly. The shock of this child's death seems to have affected the patient's mind, for according to her friends' account she immediately began to exhibit mental symptoms.

She imagined that the boy visited her in dreams at night, and conversed with her. She then failed to rally from the physical weakness in which the parturition had left her, and became very low-spirited.

This depression rapidly increased; she became restless, wandered about the house at night, could not be kept in bed, was rambling in her talk and noisy, finally could not be managed at home, so was sent to the workhouse. While there it is noted:—She is violent and restless; throws herself about, making grotesque grimaces, and staring wildly. After remaining there for four days she was admitted to Prestwich Asylum, on February 9, 1901.

STATE ON ADMISSION.

Physical Condition.—She is a small, thin, dark Jewess, very emaciated. Lungs apparently healthy. First sound of heart very faintly heard.

Her reflexes could not be examined, owing to her restlessness and resistiveness.

Mental State.—She is semi-stuporose, pays no attention to those around her, nor to questions put to her. Wanders aimlessly about her room, moaning, and shrinks when touched or spoken to, as if in fear of some impending evil.

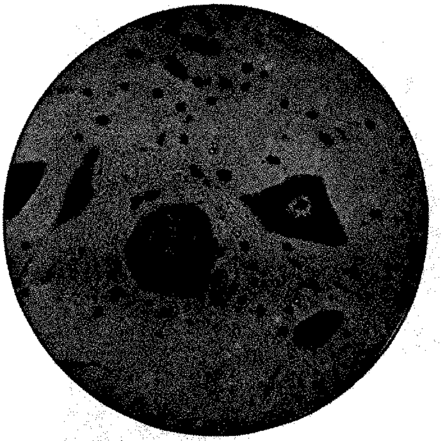
February 10. Her mental state is exactly as above. She has not slept; has been crawling round her room moaning. Heart sounds are very feeble. Dirty in her habits.

February 12, 10 a.m. This morning she is much worse, restlessness continues, and she is very resistive; cannot stand without support. At 12.50 p.m. she suddenly collapsed, fell back and died of syncope.

AT THE AUTOPSY.

The thoracic and abdominal organs were found free from any morbid change visible to naked-eye examination, with the exception of a slight congestion of the liver. The normal process of involution seemed to have taken place without interruption in the uterus. On turning to the brain, a slight milkiness of the pia arachnoid was noted, most marked in the sulci. The surface of the hemispheres presented no abnormality, and on cutting into the brain the gray matter was found to be slightly darker in colour than normal.

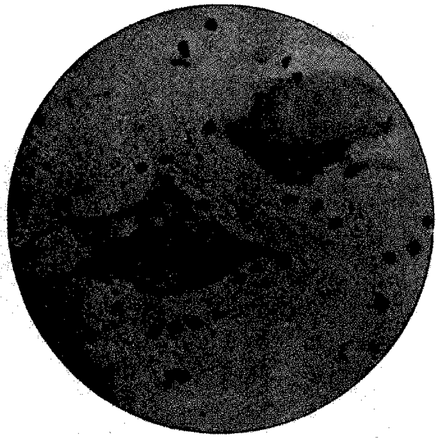
On the posterior surface of the cord there was a thin, very recent hæmorrhagic effusion underneath the pia arachnoid, and extending from the lower part of the cervical enlargement downwards as far as the upper part of the lumbar region. This effusion was very slight in degree, thin, and varied from a thread to a quarter of an inch in breadth. At no place did the hæmorrhage seem sufficient to exert pressure upon the cord.



Photograph 5.

Of the two cells in the centre of the field, the one on the left-hand side of the photo shows advanced chromatolysis. The nucleus is very pale, and a faint fringe of chromophile substance remains around the periphery of the cell.

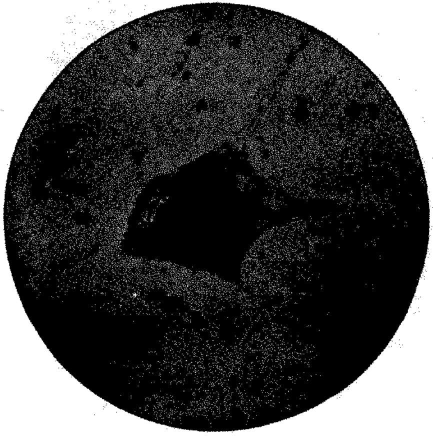
Spinal cord.



Photograph 6.

Note the vacuolation of the cell body and peripheral situation of the nucleus.

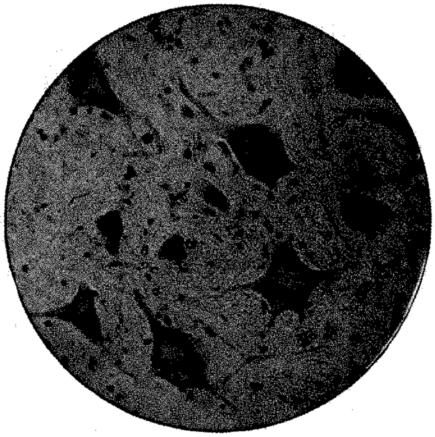
Spinal cord.



Photograph 7.

Note the vacuolation at the right hand side of the cell. The central chromophile bodies are broken up and the nucleus is peripheral. Observe the semi-lunar chromophile band attached to the nuclear envelope.

Spinal cord.



Photograph 8.

Observe the diffuse staining of the cells, indicating acute chromophile dissolution. The nucleus is markedly peripheral in position.

Spinal cord. Lumbar region.

As in Case 1, tissues from the brain, cord, and posterior root ganglia were preserved for microscopical study.

The same methods of fixation, hardening, embedding, cutting, and staining were employed as before.

Cortex.

Fronto-motor region.—Some of the large pyramidal cells do not show any definitely localised chromatolysis, but instead, a slight general fragmentary change at the edge of the individual Nissl bodies, the small detached pieces of chromophile material lying free in the fundamental amorphous substance. The great majority of the large and medium pyramidal cells, however, are readily seen to be affected by a central chromatolysis associated with pallor of the nucleus. The area around the nucleus denuded of chromophile substance is fairly extensive, and it is common to find that the peripheral chromophile elements are breaking down as well as the central ones, though to a much less degree. The nucleus maintains its central position in most instances, but when the chromolytic change has implicated the periphery of the cell to as great an extent as the central parts, the nucleus becomes excentric, and may even pass out to the edge. When this stage of degeneration is reached, the entire cell-body tends to stain somewhat diffusely, and is occupied by very minute granules of disintegrated chromophile substance. In the small pyramidal cells there is as great a degree of chromatolysis as in Case 1, but the nucleus does not show the same strong affinity for aniline dyes.

Cervical Enlargement.

Fixation in saturated sublimate and picric acid, embedded in celloidin and paraffin; stained with toluidin blue. The changes in this case are practically identical with those observed in Case 1.

There are many cells which deviate little from the normal appearance, the chromatolysis being very small in amount (Photograph 1).

In some of the large cells of the anterior cornua a well-marked perinuclear chromatolysis can be observed, and a few show a further stage of degeneration, where the entire chromophile substance is reduced to powder and stains faintly.

When this degree of chromatolysis is present the nucleus becomes peripheral in position (Photograph 4).

No cells showing the intense diffuse staining of t mentioned in Case 1 have been met with in this case, and there is less pigmentary change present.

Posterior Root Ganglia.

Fixation in saturated sublimate and picric acid; embedded in celloidin and paraffin; stained with toluidin blue.

The pathological changes in the nerve-cells are found to be precisely the same as in Case 1.

In some of the cells, which belong to the large type, very little change can be detected in either the small granuliform chromophile elements or in the peripheral ring of large elements. As noted in the preceding case, however, the nucleus of some cells which present little appreciable change seems to have a strong affinity for the stain, and colours very deeply and diffusely blue; occasionally it may undergo an atrophic transformation and be reduced to almost half its original dimensions, with the result that the perinuclear space becomes much wider than normal.

The earliest stage of degeneration in the above type of cell consists in the granuliform elements losing their affinity for the stain, and in an actual reduction in bulk of this granuliform mass.

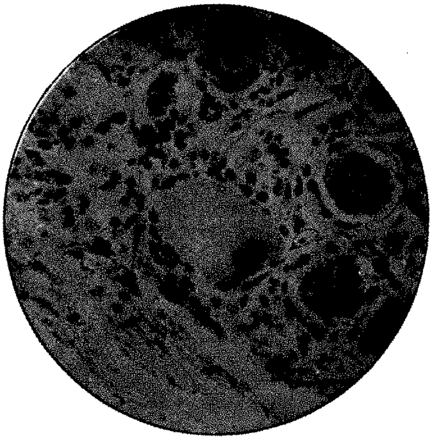
As the chromolytic process extends this central granuliform mass gradually disappears, until the centre of the cell is left quite white, surrounded by the peripheral ring of chromophile elements, which now shows evident signs of breaking up. The nucleus is pale, and although sometimes excentric, remains in the majority of instances central in position (Photograph 10).

Occasionally one sees cells in which there has been apparently a more rapid chromatolysis. The whole cell-body is completely denuded of chromophile material, stains very pale blue, and the nucleus, to which is attached a small irregular chromophile mass, is markedly excentric (Photograph 9).

The large clear vacuoles surrounded by chromophile substance are seen in this case as in the preceding one; and in the dead cells, which are invaded by the previously mentioned oval and round nuclei, one finds the vacuoles peculiar to this stage of degeneration present sometimes in large numbers.

Medullated Fibres of Spinal Cord.

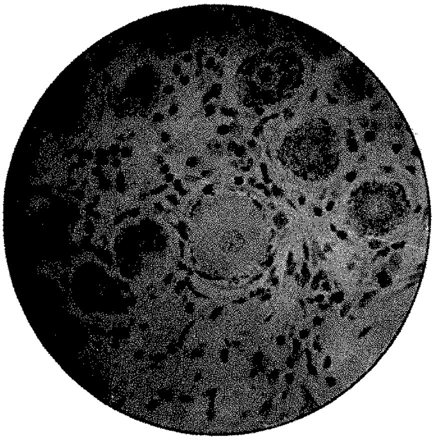
By *Wolter's method*, the crossed pyramidal tracts and the central part of the posterior columns are seen to stain a little more faintly than the other regions of the cord, on naked-eye examination of the sections. Microscopically many of the nerve-
these more faintly stained parts have lost their affinity
and their walls are thinned.



Photograph 9.

Note cell in centre of field. There is here complete chromatolysis, with excentricity of the nucleus, surrounding which is a small amorphous chromophile mass.

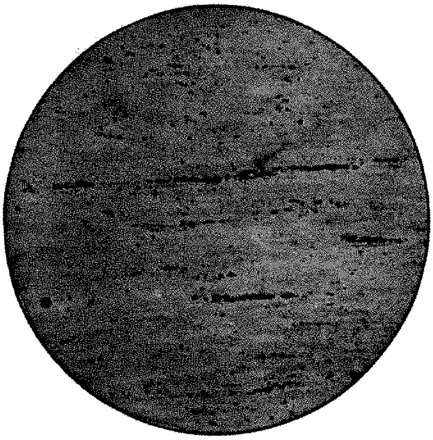
Posterior spinal root ganglion.



Photograph 10.

Note cell in centre of the field. There is here almost complete chromatolysis, a few chromophile elements being left around the cell periphery. The nucleus is central and pale.

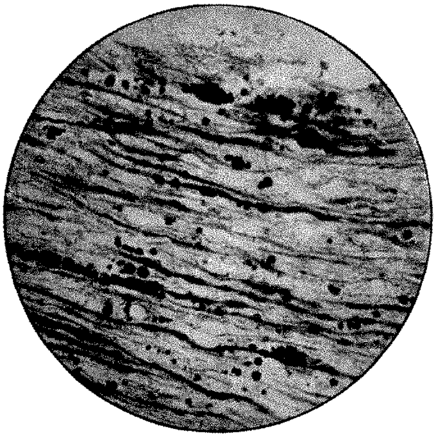
Posterior spinal root ganglion.



Photograph 11.

Observe the black droplets, indicating Marchi degeneration.

From longitudinal section of spinal cord.



Photograph 12.

Photograph from section stained by the combined Marchi and safranin method. Observe at the left and lower edge of photograph a row of Marchi droplets; elsewhere one can see myelin tubes and axis cylinders stained by the safranin.

Longitudinal section of spinal cord.

By the *Marchi method*, black droplets are found scattered over the entire cord, but, as in Case 1, the number of degenerated fibres is greater in the crossed pyramidal and posterior columns. In the grey matter there are a few black droplets scattered about, and, rarely, one sees a fibre passing from the anterior cornua to the anterior roots which yields the typical Marchi reaction.

Longitudinal sections treated by the Marchi method show here and there the row of black droplets indicating myelin degeneration. These rows are a little less frequently met with in this case than in Case 1.

Scattered throughout the field are a considerable number of black droplets, either isolated or arranged in groups of two or three.

With the *combined Marchi and safranin method* much change can be noted in the myelin sheaths.

Along the nerve the staining varies greatly, some portions colouring well, while others stain faintly or not at all.

Even in the segments where the affinity for the stain is good, one can see that the colour is not equal, small patches being more faintly stained and thinner than other adjacent ones. In certain segments the myelin is much atrophied, and only a few small faintly staining violet masses are seen surrounding the axis cylinder, which here is often flattened or ribbon-like, with it may be irregular edges, and stains exceedingly faintly. Often the marked difference in the appearance between one part of the sheath and another is well shown on either side of the nodes of Ranvier, which occasionally one notices in the course of the nerve.

On one side of the node the myelin is apparently healthy, but on the other side the myelin may stain quite faintly for a considerable length of its course, and in it the axis cylinder is flattened, irregular in outline, and of a faintly violet colour.

Sometimes, through a portion of well-stained myelin, one can see differences in thickness of the axis cylinder, and even fusiform swellings on it.

Scattered promiscuously throughout the section a few globules of degenerated pale violet staining myelin are seen.

Case 3.—M. A. H., female, aged 62, single.

HISTORY PREVIOUS TO ADMISSION.

From patient's friends no history is obtainable, unfortunately, so that one's information is necessarily scanty, and is obtained from those who brought her to Prestwich. It would appear that the patient was one of two old maids who lived together on a very slender income, and so at times suffered considerable privation.

Her illness was of about six weeks' standing when admitted here, and seems to date from the time when she sustained a considerable shock, having been a witness of her brother's death in a carriage accident. Of the onset and early course of the mental symptoms we are unable to give any data, but when admitted to this asylum her condition was one of great depression. Previous to admission she attempted suicide by tying a garter round her neck.

General Condition.—She is rather tall and gaunt. Her face wears a very anxious expression. Hair grey.

Respiratory system apparently healthy. Sounds of heart loud. Radial arteries tortuous and dilated.

Mental Condition.—November 15, 1900.—She talks readily about herself and affairs. Says she was greatly distressed at her brother's death. Admits trying to destroy herself, as she thought she was in great trouble.

On the night of her admission she slept fairly well. She never showed any signs of mental improvement, and one week after admission it was noted that she objected to taking food and was developing hallucinations of hearing, saying that the people around called her names. Soon her condition was such as to necessitate her transfer to the infirmary ward; mentally there was no improvement; she was very miserable, facial expression very dejected; there was a slight tendency to diarrhœa.

December 14.—She is utterly hopeless, gloomy, silent, and miserable; appetite very poor; no diarrhœa. During the next fortnight her general condition became worse. She remained reserved and gloomy; took no notice of what went on around her; took very little food. She continued to go down in health, and was put to bed, when her condition became rapidly worse; she became prostrate, feeble, and almost pulseless; took very little nourishment and had to be hand-fed; remained in a state of great mental depression, and finally died on February 20, 1901.

AT THE AUTOPSY.

The heart muscle was found slightly softer than normal, and there was a moderate degree of atheroma of the ascending aorta. The left lung was apparently healthy, but in the right the base was somewhat congested.

Neither the stomach, intestines, nor liver showed any morbid change recognisable by naked-eye examination. The kidneys were small—left three ounces, right four. The capsules were rather adherent, and tore the renal surface on stripping. The cortices were narrowed, calices dilated, and general renal substance much paler than normal.

In the brain the pia arachnoid was slightly milky over the surface generally, but a little more marked in the sulci. The vessels at the base were slightly atheromatous.

On cutting into the brain the little pinkish patches seen in the other cases scattered along the cortex were present.

Tissues from the fronto-motor cortex, cervical and lumbar enlargements, and the posterior root ganglia were preserved for the microscopic examination of the nerve-cells. The cord was placed in bichromate of potash 2 per cent. for the study of the nerve fibres and sheaths.

Cortex.

Fronto-motor region.—Fixation, hardening, embedding, and staining, as in the two preceding cases.

The changes in the cells of this region are similar to those already described in Cases 1 and 2. There are many large pyramidal cells and giant cells which show a small degree of chromatolysis, consisting merely in slight fragmentation of the edges of the chromophile bodies generally throughout the cell-body, whereby those bodies lose their angular appearance and become more rounded in form. There are many of those large pyramidal cells, however, in which the chromophile elements around the nucleus are broken up, and in many cases the chromophile elements at the base, while at the periphery of the cell they remain as yet unaltered. As the area of chromatolysis increases in diameter, the central portion of the cell is seen to be occupied by a pale blue, almost homogeneous mass, which on high magnification is seen to be composed of very fine granules densely packed together. The peripheral chromophile elements now show distinct fragmentary change, as also do the elements in the protoplasmic processes; the nucleus tends to pass out towards the periphery of the cell.

The medium and small pyramidal cells show the advanced stage of degeneration noted in the two preceding cases. Very deep diffuse staining of the nucleus of the small pyramidal cells is quite exceptional.

Many examples of complete destruction of the nerve-cell are met with, and small misshapen masses of cytoplasm alone remain, containing little or no chromophile substance. The nucleus is very pale in those.

Cervical Enlargement.

Fixed in saturated sublimate and picric acid; embedded in celloidin and paraffin; stained with toluidin blue.

In this region almost three-fourths of the large multipolar cells show a decided increase of yellow pigment. In some the pigment occupies almost the entire cell-body with the exception of a small band round the edge, where the chromophile elements are fairly well formed and preserved. Of true chromatolysis there are two forms, the most frequent consisting of a slight general fragmentary change involving the edges of the chromophile bodies, so that small particles are detached from them and lie free in the intervening spaces between the individual elements.

The other form of chromatolysis is much less frequent than the above, and is a true central chromatolysis. The perinuclear chromophile elements are reduced to powder, while around the cell periphery and in the protoplasmic processes the chromophile substance is plentiful and well formed; the nucleus remains central.

There are no diffusely-stained homogeneous-looking cells, such as are found in Case 1.

In the small cells, scattered throughout the grey matter of the anterior and posterior horns, the chromophile elements are broken throughout the entire cell body, and stain faintly.

Lumbar Enlargement.

The sections were prepared in exactly the same way as those from the cervical enlargement.

In the large multipolar nerve-cells, the fragmentation above noted is present.

In a few cells, the chromophile elements show the rounding of outline and the small detached portions of chromophile substance lying between the individual elements, as in the cervical enlargement.

The great majority of cells, however, show a fairly advanced central chromatolysis. The perinuclear chromophile elements are broken up into a fine dust, which stains very deeply; the elements at the periphery are well preserved. At this stage the nucleus is central.

As the change advances outwards, involving the peripheral zone of the cell, the central part stains more faintly and in a somewhat diffuse manner, while the peripheral chromophile substance shows evident signs of disintegration. The nucleus now is excentric, and occasionally one sees a deeply-stained semilunar chromophile band attached to the outer side of the nuclear envelope on that side of the nucleus which looks towards the centre of the cell (see photograph 7). There are no homogeneous-looking cells as in Case 1. The small nerve-cells scattered throughout the grey matter stain more faintly than the larger ones, and while some show a distinct central chromatolysis, others are entirely denuded of chromophile substance.

Posterior Root Ganglia.

The ganglia were fixed, embedded, and stained in exactly the same manner as the slices from the cervical and lumbar enlargements.

A very considerable number of the large cells present an extremely slight degree of morbid change, which consists merely in a slight loss of affinity of the chromophile elements for the toluidin blue, whereby the minute granules in the centre of the cell appear less distinct than normal.

In those large cells, however, various degrees of chromatolysis are met with, from slight central chromatolysis to an advanced stage, where only a ring of chromophile elements is left around the margin of the cell. The nucleus remains for the most part central.

In the medium-sized cells, with large chromophile elements, central chromatolysis, with marked excentricity of the nucleus, is the rule.

As in Case 2, cells are found where there seems to have been a very rapid degenerative process. The cell is almost entirely denuded of chromophile substance, and stains very faintly blue, the nucleus is peripheral in position, and may have attached to the side of its nuclear membrane a mass of amorphous chromophile material, which represents all that is left of the Nissl granules. The outline of those cells is always quite regular (photograph 9).

Dead cells are fairly frequently met with, in which the cytoplasm is broken up and vacuolated, and contains oval or round nuclei which have wandered in from outside.

As in the spinal cord, the amount of pigmentation in the nerve-cells of the posterior root ganglia exceeds the normal physiological limits, and consists of two varieties, viz., a yellow-coloured pigment and a pigment of a greenish hue.

Homogeneous atrophy of the nucleus, a condition which will be described later, is fairly frequently met with in this case, and is found in cells which present a marked affinity for the stain and colour very intensely. The chromophile elements are almost entirely obscured, and seem fused together to form a deep-staining homogeneous mass. The nucleus can be made out small and stained deeply, showing no detail of structure. In the centre lies the nucleolus, which is coloured rather more strongly than the atrophied homogeneous nucleus.

Medullated Fibres of Cord.

By *Wolter's method*, sections on naked-eye examination show a slight pallor of the crossed pyramidal tract on both sides, just as in the two preceding cases.

In the posterior region the staining is fainter in both external and internal columns. In the external column the loss of affinity for the stain affects the anterior two-thirds, and the fibres nearest the posterior horn and those next the internal column stain more strongly than those in the centre. In the internal column the fibres around the postero-median septum stain more lightly than the more externally situated ones, and the pale area is more evident around the anterior half of the septum.

Microscopically the tubules in the paler areas are seen in many instances to be only partially stained, and many are atrophied.

By the *Marchi method*, one finds degeneration in the form of scattered black droplets, which are most numerous in the crossed pyramidal tracts and in the posterior columns, although they occur in considerable numbers in the anterior and antero-lateral columns as well.

There is a slight amount of degeneration in Lissauer's tract, and many small black dots are seen in the grey matter. The amount of degeneration in this case is a little more than in Case 2.

Rows of black degenerated myelin drops are seen in the longitudinal sections prepared by the Marchi method, and occasionally the altered myelin sheath at certain points is fused into a long slender black mass. Many black droplets of varying size are scattered over the field.

By the *combined Marchi and safranin method*, the earlier stages of myelin atrophy such as are described in Cases 1 and 2 are seen here also, but in many fibres there are long tracts of the nerve in which the myelin is unstained, and persists only as shreds joined to each other or detached, leaving the axis cylinder practically bare. This latter structure stains very faintly, and varies in thickness in its course. At some points there are fusiform swellings, the edges of which stain a little more strongly than the centre, as if the fibre had been split longitudinally into two portions in this situation. Some fibres are less affected, and large parts of myelin stain well, but between two well-stained portions the intervening myelin is thinned, and stains a faint violet colour. In some violet staining parts there are distinct roundish vacuoles, but in other places the myelin may be almost completely atrophied, more along one side of the axis cylinder than on the other, for some distance.

A row consisting of several pale violet staining beads may represent all that remains of the myelin sheath, and the axis cylinder is left naked, pale, and ribbon-like. It is occasionally observed that a small segment of myelin yields the black Marchi reaction, and on either side of it the sheath stains red, and is apparently unchanged.

Case 4.—J. L., aged 34, single, a labourer.

HISTORY PREVIOUS TO ADMISSION INTO THE ASYLUM.

Previous to his admission into the Workhouse nothing is known regarding the patient.

In the workhouse, where he was detained for three days, it was noted :—He is confused, memory very defective, has no idea of time, nor does he know where he is.

STATE ON ADMISSION.—(*December* 3, 1900.)

He is a man of medium height, in fair physical condition. Lungs healthy. Heart regular. Patellar, plantar, and pupillary reflexes quite normal. Tongue tremulous.

Mentally he is very dull, stupid, and confused. Memory poor. Does not know where he came from, nor the day of the week. Has delusions of persecution, and cannot sleep for fear of men attacking him.

December 5.—Very impulsive; constantly jumps out of the chair; tries to run away, saying he is about to be murdered.

Sleeps fairly well; appetite good.

December 12.—Restless and delusional as before. Given chloral, grains 15, and potassium bromide, grains 20, twice daily. Appetite good.

December 19.—No better during daytime, sleeps better at night.

December 26.—Quieter and more tractable.

January 20, 1901.—Again excitable, restless and noisy.

February 20.—Restless and bad-tempered; surly in disposition; generally incoherent.

March 30.—Remains unchanged and continued excitable, restless, noisy and intractable until June 3, when he developed physical symptoms of a grave character, which ultimately led to a fatal issue.

June 3.—He is suffering from diarrhœa. Temperature 105°. Stools liquid and brown-coloured; no slime or blood in the discharge. Given chinosol, 2 grains per diem.

June 5.—Diarrhœa rather better. He has some dyspepsia. Sleeps fairly well. Takes nourishment well.

June 6.—Signs of consolidation at base of left lung, extending up as far as the angle of the scapula. Little cough; no expectoration.

June 8.—Marked pneumonia, with all the symptoms. Much less diarrhœa. Pulse small and rapid. Respiration rapid.

June 9.—He is delirious. Heart is failing. Sleeps little.

June 10.—No abatement in the symptoms. Died at 4.40 p.m.

His mental symptoms remained of an acute nature until the end.

AT THE AUTOPSY.

Heart weighs 15 ounces; both right and left sides are dilated, and the muscle softer than normal. One ounce of fluid in the pericardial sac.

Right lung weighs one pound eleven ounces. There is considerable congestion at the base, and œdema generally throughout.

Left lung.—The entire lower lobe and three-fourths of the upper lobe show pneumonic consolidation, which has reached the stage of grey hepatisation.

In the stomach and small intestines no lesions were found, but in the large intestine, at its lower end, just above the sigmoid flexure, there were two small round ulcers, with thickened and rather firm edges.

The liver weighed five pounds, and was greatly enlarged and congested. Spleen 4½ ounces.

The capsules of the kidneys stripped easily, and there was no morbid change visible to the naked eye.

In the examination of the brain there was little to be seen on naked-eye examination. The pia arachnoid was slightly milky, and on cutting into the brain the grey matter generally was rather pinkish and hyperæmic-looking.

The following tissues were preserved. Slices from the cortex—fronto-motor region—and from the cervical and lumbar enlargements. The entire cord was preserved for the examination of the medullated fibres and axis-cylinders. No posterior root ganglia were preserved from this case.

Fronto-motor Cortex.

Fixation in saturated sublimate; stained by Robertson's methyl violet method and by toluidin blue.

In the large and medium-sized pyramidal cells the type of chromatolysis differs very markedly from that observed in the three preceding cases, where it is perinuclear, or sometimes basal, at first, and seems to extend with comparative slowness outwards towards the periphery.

In this case, the degree of chromatolysis is much greater in the cell itself, and also in the number of cells affected.

All the cells stain in a diffuse manner, as if the chromophile elements had been dissolved, instead of showing the fragmentary appearance which is found in the three preceding cases. The cells stain more deeply than usual, and the colour is uniformly distributed throughout the cell. This uniform colouration might be explained by the fact that the amorphous fundamental substance of the cell-body is probably reinforced by the dissolved chromophile substance. The cell outline remains unchanged, and the protoplasmic processes, which are devoid of formed chromophile substance, stain diffusely blue, and can be followed for a considerable distance.

Although this description holds good for practically all the cells, one does encounter an occasional cell in which a few small granules of chromophile material are present. Those granules when present are always situated at the periphery of the cell, which seems to support the view that the degenerative change probably begins, and is at the first more intense, in the perinuclear and central regions of the cell-body.

The nucleus usually stains a little paler than normal, and retains its central position in the large majority of instances, although at times, where the cell is very degenerated, and has become pale and ghostlike, it is common to find the nucleus quite as pale as the cell-body, and closely applied to its periphery.

If one examines the above-described diffusely-stained cells with high-power apochromatic lenses, a fine network is visible.

This network is composed of faintly-stained meshes of equal size, and extends uniformly throughout the cell body. This has only been observed in sections stained with toluidin blue. In the nucleolus there is a very unusual appearance to be seen. The nucleolus, while retaining its rounded shape, seems to be vacuolated, as many as five or six small transparent vacuoles being observed, separated by well-stained partitions radiating out from the centre.

Many cells are observed so faintly stained as to earn the term "ghost cells." Their outline is very faint and irregular, and the nucleus is barely discernible. In addition to these cells, one can see small masses of pale, thin protoplasm, which are cell residues. The small pyramidal cells are much more faintly stained than the larger ones; their processes are completely destroyed in many instances, and they seem to have succumbed to the degenerative change much more quickly.

Lumbar Region.

Fixation in saturated sublimate and picric acid mixture; embedded in celloidin and paraffin; stained by toluidin blue.

In some of the cells of this region there is a small collection of yellow pigment, which in quantity rarely exceeds physiological limits. A small number of the large cells show very little of a morbid nature, the change being limited to a slight fragmentary change affecting the edge of the chromophile elements throughout the cell-body generally.

The typical change present in the majority of cells consists of a central chromatolysis.

The fragmentary change may occasionally be limited to the immediate neighbourhood of the nucleus, but much more often the entire central portions of the cell are affected, the chromophile material being broken up into a fine dust around a central nucleus.

In the protoplasmic processes, and at the margin of the cell, the Nissl bodies are well preserved. Some cells may show well-marked vacuolation in their interior. In these cells the chromatolysis is more advanced; the peripheral chromophile elements persist, it may be, as a single row, while the centre of the cell is occupied by a very fine chromophile dust. The vacuoles are clear, transparent, and round, with well-defined outline, and may vary in number from three to six in a single cell. The nucleus, though well stained, is always excentric, and on the side turned towards the centre of the cell, the nuclear membrane may be indented, and in the cavity so formed one finds a small semilunar band of chromophile material (photographs 6 and 7).

Of the small nerve-cells scattered throughout the grey matter of both anterior and posterior horns, some show little change, others well-marked central chromatolysis, and others are completely denuded of chromophile substance, *i.e.*, in a condition of achromatosis.

Medullated Fibres of Spinal Cord.

In transverse sections stained by *Wolter's method,* the areas which take the stain with less intensity are identical with those in the last case. By the *Marchi method,* black droplets are seen scattered throughout the field, but in the crossed pyramidal tracts and in the posterior columns they are more numerous than in other situations.

In the anterior horns, especially in the lumbar region, one can see some of the fine medullated sheaths showing the black reaction. In longitudinal sections of cord, long and short rows of black globules indicate myelin degeneration, the number of degenerated fibres being about the same as in Case 3.

With the *combined Marchi and safranin method,* the previously-mentioned atrophy of the sheath is well shown, which in many fibres may leave the axis-cylinder denuded for a considerable [illegible] of its length.

Round globules of altered myelin are found, which stain a [illegible]intly violet tinge.

On some fibres there sometimes occur black dots scattered at [illegible]rregular intervals, which clearly indicate foci of degeneration. Several of those dots may run together to form a small globule, and are present both in well-stained portions of sheath or in myelin which is atrophying. Such small foci yielding the Marchi reaction are fairly commonly encountered.

The changes in the axis-cylinders of this case are identical with those seen in the first three cases.

Case 5.—J. H., aged 39, married.

HISTORY PREVIOUS TO ADMISSION.

Patient has always been a hard-working man, but recently has been greatly worried concerning certain of his business affairs. No mental symptoms were noted by his friends until six days ago, when he became very restless, depressed, and latterly excited, and threatened to harm himself. He was taken to the workhouse, where he remained four days, and while there his mental state was as follows :—" He says he is not fit to live; he has deceived himself and everybody around him; he has a dejected manner and furtive look at times."

His memory for past events was poor. Patient was admitted to Prestwich Asylum on May 23, 1901.

Physical State.—Fairly tall man. Lungs normal. Heart normal. Knee-jerks brisk. Pupils normal.

Mental State.—Very depressed, restless, and excited; rarely speaks, says he wishes to die; is very fearful, won't remain quiet, and rushes wildly about his room. Sleeps very badly.

May 24. Very restless, tries to break away or lies down on ground; last night he butted his head against the door and bruised his scalp. Given milk, eggs, and whiskey.

May 26. Very depressed, and has to be fed with the tube; rarely speaks; very resistive; restless, and out of bed most of the time; has lucid intermissions.

May 28. Is taking his food a little better, otherwise unchanged.

May 30. Pulse not so strong, and there is œdema of the feet and legs. Given milk, eggs, and whiskey—8 ounces per diem.

June 3. Œdema has disappeared, and he is taking his food much better; he is mentally as before; his temperature is frequently 99.2° to 99.8°.

June 8. Condition remains practically the same. Temperature sometimes up to 101° in the evening and occasionally raised [illegible] the morning.

June 9. Up and down temperature persists. His bowels a[illegible] rather frequently, but that is due to doses of calomel. N[illegible] abdominal tenderness nor distension; no increased dulness [illegible] spleen; no lung symptoms. Mentally he is stuporose, with a tendency to catalepsy. He has to be fed; swallows with difficulty. Passes urine in bed. Given milk, eggs, and whiskey.

June 10. Mentally much the same. Tongue dry and coated; no diarrhœa. Sleeps fairly well.

June 11. Much worse this morning. Face cyanosed. Marked dyspnœa, crepitations over right lung. Pulse small, quick.

Died exhausted at 1.25 p.m.

AT THE AUTOPSY.

The lungs were healthy to naked-eye examination. The heart weighed 9¼ ounces; muscular walls firm and of good colour; in the aorta there were several small patches of atheroma. The stomach and small intestines presented no pathological change appreciable to the naked eye, but on examining the large intestine a profound lesion of the mucous coat was found to be present.

At the upper end there were numerous small white scars scattered irregularly over the mucous surface. Half way down the gut and as far as the sigmoid flexure there was an intense ulceration. Some of the ulcerative patches were three inches in length and about half an inch in breadth; others were smaller, varying from a quarter of an inch to one inch in length. Those ulcers varied in shape, some being roundish, others oval, and all were of considerable depth.

The liver, beyond some congestion, showed no morbid change to naked-eye examination, nor did the spleen or kidneys show any appreciable alteration.

The pia arachnoid was very slightly milky, and the brain itself presented no morbid appearance beyond some pink patchy infection of the grey matter of the cortex.

The usual tissues were retained for microscopic study.

Cortex.

Fronto-motor Region.—Fixation in saturated sublimate. Stained by Robertson's methyl violet method, and by toluidin blue.

The description of the cortical cells in Case 4 applies precisely to the large majority of the cells in this case.

The deep blue diffuse staining of the cell-body, due to [illegible]ssolution of the chromophile material, is present. Cells thus [illegible]anged show either no formed chromophile material or faint [illegible]aces only of such. In the diffusely-stained cell-body a net-work identical in form to that noted in Case 4 is seen, and in addition one can see in this case minute clear vacuoles in certain of the cells.

But this case differs from the preceding one in that a limited number of large pyramidal cells are comparatively little affected by the chromolytic change. Their chromophile elements are only slightly diminished in number, but the outlines of those bodies are irregular, shadowy, and look as if their edges had been dissolved away.

Further, the fundamental amorphous substance of the cell is more highly stained than normal. In the nucleolus one occasionally observes the vacuolated appearance referred to before, and in the nucleus the staining is good except where the cell itself is very pale.

The appearance of the pale, ghostlike cells found in this case, and of the small pyramidal cells, are identical with those noted in Case 4, so that any further description of them is unnecessary.

Cervical Enlargement.

Fixation in saturated sublimate and picric acid; embedded in celloidin and paraffin; stained by toluidin blue.

Many of the large cells in the anterior horns show little alteration. The chromophile bodies stain well and are very slightly fragmented at their edges. In some cells there is an accumulation of yellow pigment, which does not, however, exceed the normal physiological quantity except in a few isolated instances.

In a large number of the cells a central chromatolysis is present. Here one finds an area, around the nucleus, pale blue and diffusely stained, in which the minute fragments of broken chromophile material are with great difficulty seen.

As one passes out towards the cell periphery fine chromophile granules make their appearance, and finally, at the margin of the cell, the best preserved elements are found, showing either normal contour or commencing fragmentation. At the beginning of the chromatolysis a hyperchromic band may be seen surrounding the nucleus. This band can be seen with high powers to be composed of very fine fragments of chromophile material densely packed together. When the process of chromatolysis has reached an advanced stage, the zone surrounding the nucleus is often quite denuded of chromophile substance, and stains in the fainte[illegible] manner possible.

In the early stages of the degenerative process the nucleus [illegible] pale, with a well-stained nucleolus, and retains its centr[illegible] position; but later, when the process has involved the entir[illegible] cell, with the exception of a narrow peripheral zone, one finds the nucleus pale, excentric, or it may be at the extreme margin of the cell.

Sometimes that part of the nuclear membrane which looks towards the centre of the cell is indented, and in the concavity so formed a small mass of deeply-stained chromophile substance lies.

In the advanced stage of chromatolysis the protoplasmic processes are devoid of chromophile material and very pale.

The small nerve-cells in both anterior and posterior horns are much paler than the large ones. Many stain diffusely blue, and show no trace of formed chromophile substance; others show a few scattered granules. The nucleus is pale, but the nucleolus stains well.

Lumbar Region.

Fixation, embedding and staining as in the case of the cervical enlargement.

As in the cervical region, cells are seen showing little appreciable change; the presence of pigment in some of the cells is to be noted also.

There are many cells, however, which are gravely altered. In those which show the least amount of degenerative change one finds the perinuclear region much more intensely coloured than the other parts of the cell. With high powers, this hyperchromic region can be seen to be composed of finely granular broken-down chromophile material, the granules being densely packed together and giving the intense colour referred to.

The peripheral elements, meanwhile, are practically regular in outline and of normal staining reaction.

A further stage is seen where the central chromophile elements become reduced to a fine dust and stain with much less intensity; at the periphery only a fringe of chromophile substance is left, consisting of well-stained elements, one or two of which, however, may show fragmentary change.

In the protoplasmic processes the chromophile elements are as yet normal.

The nucleus is pale, central, and the nucleolus shows no change.

As the cell becomes still more degenerated, both central and peripheral chromophile elements are reduced to a fine dust, a few formed granules alone remaining in the protoplasmic processes, and at the extreme margin of the cell. The nucleus now takes up a peripheral position, and is very pale.

Sometimes the chromatolysed perinuclear zone of affected cells stains diffusely and pale blue, as if the chromophile substance had been dissolved instead of being broken up. This change is a late one in the degeneration of the cell, as the peripherally situated elements and those in the protoplasmic processes are broken down into granules and stain more faintly than normal. The nucleus here is very pale and markedly peripheral, and in its interior no detail of structure is perceptible. The process of dissolution may in some cases spread to the periphery of the cell, leaving it pale, indistinct, and homogeneous-looking, with a mere shadow of a nucleus.

In the small nerve-cells scattered throughout the grey matter complete chromatolysis is the rule, but a few may show a marginal chromatolysis only, in which the cell periphery and processes are denuded of chromophile substance and stain homogeneously pale blue, while the central parts are occupied by fragmented granules weaker in staining reaction than normal.

It is seldom that one sees examples of peripheral chromatolysis like the above.

Posterior Spinal Root Ganglia.

Fixation, embedding, and staining as in cord.

The cells of the posterior root ganglia in this case present a very marked degree of degenerative change—much more so than has been observed in any of the preceding cases. In fact, there are extremely few cells which one can speak of as normal. In the cells which normally have granuliform chromophile elements throughout the cell, and in those which possess in addition a peripheral ring of large elements, one finds varying degrees of change. At first, the minute chromophile granules decrease markedly in number in the centre of the cell, giving to it a pallid appearance, and the nucleus stains more faintly with the toluidin blue. This degenerative change advances, and when the peripheral ring of large elements is present it is seen to undergo fragmentary change also, and ultimately to disappear as well as the central elements. The cell thus gradually assumes a very pale blue or bleached appearance, and the nucleus, which with few exceptions remains central, loses its affinity for the stain and its internal details of structure disappear. Occasionally it happens, however, that instead of finding a pallid nucleus in those cells, one observes it shrunken and stained diffusely and very deeply, showing the typical appearance of homogeneous atrophy.

Many of those pale achromatosed cells are liable to nuclear invasion, and it is common to find round or oval nuclei buried in the cell cytoplasm.

In the medium-sized cells, which normally contain large chromophile elements, one finds a typical central chromatolysis.

The centre of the cell is occupied by fine, deeply-stained chromophile dust, while the elements at the periphery are not affected to such a degree, although far from normal. The nucleus rapidly assumes a peripheral position.

Vacuolation of the cell is met with infrequently. The vacuoles are for the most part large, and may in some cases occupy two-thirds of the cell-body.

Medullated Fibres of the Spinal Cord.

In sections stained by *Wolter's method*, there is lighter staining of the fibres in the crossed pyramidal tracts and in the postero-internal columns. Microscopically, many myelin sheaths in these areas are seen to be thinner than normal.

With the *Marchi method*, many scattered black droplets are seen in all the tracts of the cord, and only in the posterior columns is there any appreciable increase in numbers.

In longitudinal sections Marchi degeneration is found, as in the previous cases.

By the *combined Marchi and safranin method*, atrophy of parts of the myelin sheath is observed, with intervening segments well stained and apparently uninjured.

Many sheaths are so atrophied and vacuolated as to be hardly distinguishable, and in the centre runs a pale and attenuated axis-cylinder. Some of those vacuolated segments may be of considerable length, as observed in Case 4. At some points in the nerve the medullated sheath yields the Marchi reaction. The parts affected vary considerably in length, and on either side of them no appreciable morbid change may be found.

Case 6.—E. A., aged 34, unmarried, cotton-weaver.

HISTORY PREVIOUS TO ADMISSION.

Patient was always healthy and fit for work until six years go, when she suffered from a sharp attack of rheumatic fever, om which she recovered, but with impaired health. She became y anæmic and weak, and during the last four years she has n liable to faint on any unusual exertion, so that her previous pation became impossible. Her mother states that frequently had diminished power in her limbs for slight periods of time, her sleep at night was very fitful and broken.

About the beginning of May, 1901, she became restless at night, slept very badly, and at times wandered about the house. On May 8 she had a convulsion, which, according to the mother's account, was of a general character. Her restlessness increased, and she gradually became excited and noisy, so that her removal to the workhouse was considered necessary. There her mental condition became worse; her conversation was rambling and incoherent, she could not answer questions put to her, and had exalted delusions, saying that she owned plenty of money. At the end of fourteen days she was admitted to Prestwich Asylum, on June 24, 1901.

General Condition.—A very thin woman, of medium height; fair hair, blue irides, right divergent squint. Lungs apparently healthy. Heart sounds pure, but action very rapid and feeble. Urine free from albumen.

The patellar reflexes were much exaggerated, and equally so on both sides. Her lower limbs were very weak, so that she could barely walk without support.

Mentally, she suffers from considerable confusion, cannot understand questions put to her, answering at random, and repeating the same sentence over and over again. She has no idea where she is, or from whence she came. On account of her confusion, sensation cannot be tested.

For three days after admission she remained in much the same mental and physical state, but on June 28 the degree of mental confusion was more marked; her attention could not be engaged. She rambled constantly, muttering to herself.

June 29.—Heart's action very feeble. She seems to have difficulty in swallowing. Constant restlessness, twitching of arms and legs, nystagmus.

June 30.—In much the same physical condition. Restlessness continues, and difficulty in swallowing greater. Her patellar and elbow reflexes are as exaggerated as on admission. Her eyes were examined ophthalmoscopically, and in spite of the difficulty on account of nystagmus, the following appearances were noted:—The papilla is congested and swollen-looking; the margin very hazy and indistinct, and the veins much engorged.

On July 1 her physical condition was worse. Temperatur 101·8° in the morning, 101·6° in the evening.

July 2.—Still weaker. Seems quite prostrate. Lies in [illegible] with twitching arms and legs. Reflexes still exaggera Mentally she is comatose. Temperature 101° in the morn 103·2° in the evening. She never rallied, and died at 4.30 a on July 3.

From the date of admission to the patient's death, there wa always present a general paresis of all the muscles, both of the trunk and limbs.

This did not affect one group of muscles more than another, but increased with the course of the ailment.

AT THE AUTOPSY.

The heart, lungs, intestines, liver and kidneys showed nothing of a pathological nature to naked-eye examination.

The pia arachnoid was very slightly milky over the vertex.

On cutting into the brain, the cortex was noted to be hyperæmic and pink-looking generally throughout the convolutions.

On examining the cord, marked hyperæmia was seen in the lateral parts of the cord, especially in the situation of the crossed pyramidal tracts in the cervical region.

This appearance was much less distinct in the dorsal and lumbar regions.

The following tissues were reserved for microscopical examination.

Slices from the fronto-motor region from both sides of the brain.

A portion of the cervical and lumbar enlargements, the posterior spinal root ganglia.

All those tissues were examined for nerve-cell changes. The cord was placed in bichromate of potash 2 per cent., and examined for myelin-sheath and axis-cylinder degenerations.

Cortex.

Fronto-motor Region.—Fixation in saturated sublimate; stained by Robertson's methyl-violet method, and by toluidin blue. Better specimens were obtained by the latter method in this case.

The cortical nerve-cells are more profoundly affected than in any of the preceding cases.

Every cell without exception shows an entire absence of chromophile granules in the interior of the cell-body and in the processes.

The degenerative change has advanced to such a degree that he chromophile material seems to be entirely dissolved throught the whole cell-body, causing it to assume a uniformly blue, mogeneous appearance.

The depth of staining is not equal in all the cells. In some cells the diffuse staining is very intense, and all detail in the cytoplasm is obscured, even to high powers of the microscope.

The nucleus is seen as a dense blue, oval body, in which the nucleolus is only faintly visible. The nuclear network is quite obscured, and the nucleolus is visible only on account of its intense affinity for the stain. Usually the nucleus occupies a peripheral position.

Other cells do not stain so deeply. They are diffusely pale blue, and in the cytoplasm, and for some distance along the protoplasmic processes, one can recognise a network, the spaces of which are for the most part of equal size, but here and there those spaces are wider than usual, and of irregular shape, as if rupture of the wall of adjacent spaces had taken place.

Clear, medium-sized vacuoles are present frequently. They may be round or oval, and lie for the most part towards the base of the cell; but one may meet with them in other situations.

As before mentioned, the nucleus is most commonly peripheral, and one occasionally sees a crescentic indentation of the nuclear membrane on that side of the nucleus which looks towards the centre of the cell.

The vacuolation of the nucleolus, referred to earlier, has been seen in this case also.

The paler the cell-body stains, the fainter does the nucleus become also, and many cells are so pale that their outline is only recognisable with very high magnification. The above-mentioned network can then be seen only with great difficulty; the nucleus is very pallid, no network nor nucleoli being recognisable. Small fragments of practically colourless protoplasm indicate complete destruction of cell life.

In both grey and white matter, the arterioles and capillaries are greatly engorged.

Cervical Enlargement.

Fixation in saturated sublimate and picric acid; embedding in celloidin and paraffin; stained by toluidin blue.

There is in this situation the same profound degree of change in the nerve-cells as observed in the cortex cerebri.

Even with a low power, one is struck by the absence of formed chromophile material of definite shape in the cell-body.

With a high magnification the following changes are recognisable:—There are a very few cells in which formed chromophil elements are present, small particles being scattered throughou the cell body, both centrally and peripherally, in such a manner that wide spaces are left between each.

Between the particles, the fundamental amorphous substance stains very lightly, and no detail of structure is visible.

The nucleus is pale, and occupies an excentric position, while the nucleolus is distinct, and stains well.

In ninety-five per cent. of the cells a much more grave degree of change is found.

There seems to have been here a rapid dissolution of the chromophile elements, causing the cell to assume a blue, homogeneous appearance, which varies in degree in different cells, some cells being entirely homogeneous, while in others a few minute particles of the chromophile elements are left (photograph 8). Those remains of chromophile elements are found, with the exception of a very few isolated instances, at the periphery of the cell. In those cells, around the nucleus which is peripheral, and in the central parts, the cytoplasm is homogeneously pale blue in colour, but at the extreme periphery one finds a fringe of small broken-down chromophile particles. The nucleus, as before mentioned, assumes a peripheral position, is extremely pale, and its network is unstained. The nucleolus stains strongly.

The extreme tortuosity of the protoplasmic processes is worthy of note. We have in the above description of those cells strong evidence that the process of disintegration has commenced, and advanced further in the perinuclear and central parts of the cell, seeing that the peripherally-situated chromophile bodies are the last to remain.

Many cells are met with showing a still more advanced stage. The cell stains almost uniformly pale blue, and no trace of the chromophile bodies is to be seen, but at the cell edge the homogeneous blue colour is a little more intense than in the central parts, and no details are visible in the cell-body. The nucleus is very pale, situated at the periphery of the cell, and the nuclear network is unstained. Many cells are so lightly stained that their recognition is only possible with extremely high powers. The cell-body and nucleus are reduced to mere shadows.

While the majority of these homogeneous-looking cells show no detail of structure in the cell-body, there are a few in which a distinct reticulum is visible with high magnification.

The reticulum is present in the cell-body, and extends for a ttle distance along the base of the protoplasmic processes. The reads composing the network stain deeply, and the spaces osed by them are for the most part of equal size, but here and re throughout the cell the walls of adjoining spaces are ptured, leaving clear structureless round or oval cavities in the ell-body. In these cells there are no traces of chromophile substance, although where the strands forming the reticulum are a little thicker and more distinct than usual, one may be justified in assuming that some dissolved chromophile substance is applied to the sides of the strand.

It is specially interesting to note that in the above-described cells showing a distinct cell network, the nucleus is in a condition of homogeneous atrophy. It stains very diffusely blue, is homogeneous, showing no nuclear network, but a deeply-stained nucleolus, while the nuclear membrane may be much crenated, and its actual size greatly reduced.

Lumbar Enlargement.

Fixation, embedding and staining precisely as in the cervical region. The appearances in this part of the cord are almost identical with those found in the cervical enlargement.

In a few cells one finds fine fragments of chromophile elements scattered irregularly in the central parts of the cell, while larger irregularly-shaped fragments are found towards the periphery.

The nucleus is pale, and the nuclear network unstained, while the nucleolus stains strongly with the aniline dye.

In the majority of the cells there is nearly complete dissolution of the entire chromophile material, the entire cell-body staining diffusely blue; but in the protoplasmic processes, and at the extreme edge of the cell, a few fragments of chromophile substance remain.

Cells showing a further stage of this process are seen where even the peripheral chromophile elements and those in the protoplasmic processes are completely lost. Such cells show a homogeneously blue centre and periphery, but the colour is somewhat deeper in the latter situation. No network is visible in the cell-body of those cells.

In this region, as in the cervical enlargement, there are a few cells in which a reticular structure is visible with high magnification. Rupture of the strands forming the meshwork can be seen, and often one finds in those the homogeneous atrophy of the nucleus previously described.

Tortuosity of the protoplasmic processes is again a noteworthy feature in the degenerative process, and the vascular engorgement is here present as in the other situations described.

Both small and large nerve-cells are affected to the sa extent by the acute disintegrative process.

Posterior Root Ganglia.

Fixation in saturated sublimate and picric acid; embedding in celloidin and paraffin; stained with toluidin blue.

The degree of chromatolysis present is greater than in any of the ganglia examined in the other cases, and in the sections under medium powers the cells present a pale "washed-out" appearance. In order to study the chromophile elements of those cells, it is necessary to examine carefully with very high powers, as the degenerative process here has been of a much more acute type than we have previously studied. In none of the ganglia examined are there any cells unaffected by the chromolytic process. In the large cells, which normally contain granuliform elements, and in those which also possess a peripheral ring of elongated elements, a distinct change is found.

The fine granuliform chromophile elements in the centre of the cell become reduced to an exceedingly fine dust, which with medium magnification is not visible, and the peripheric chromophile ring is no longer recognisable.

But in many cells the change has advanced farther, and now the fine central granules no longer persist, the cell centre staining very diffusely and faintly, while at the periphery there is a ring of more intense colour, in which a few minute granules can be made out, indicating the former site of the peripheral ring. It is remarkable how frequently one finds the perinuclear clear space quite obscured, as if the dissolved chromophile substance had passed into it along the cell canaliculi which normally empty into it. The nucleus is pale, with the nucleolus distinct, and frequently occupies an excentric or peripheral position. Occasionally early homogeneous atrophy of the nucleus is seen, the staining being deep and diffuse, obscuring the reticulum.

In the cells which normally possess large, well-shaped chromophile elements, one finds a definite and well-advanced central chromatolysis.

The centre of the cell is pallid, and colours diffusely blue, while at the periphery and around the nucleus, which has become excentric, a faintly-staining mass of finely-broken chromophile dust persists. In some of those cells the nucleus may be pale; in others early homogeneous atrophy is present, and occasionally he nuclear atrophy may be very advanced, even reaching the age where the nucleus is intensely coloured and much reduced n size, with a markedly crenated margin.

Some cells, comparatively few in number, are observed to ssess a very strong affinity for the dye, staining deeply and ffusely.

With the highest magnification, one observes that the chromophile material is reduced to a very fine dust, scattered generally throughout the cell, or it may even be wanting altogether. In the cell-body a distinct network is visible, whose spaces are of equal size throughout. The nucleus of those cells is always affected by homogeneous atrophy. It is greatly reduced in size, with a very irregular edge, stains so deeply as to totally obscure the nuclear network, and the nucleolus is only faintly discerned through the deep staining mass. Clear vacuoles are sometimes present in the degenerating cells. They are small and irregularly distributed for the most part, but occasionally one meets larger vacuoles, in the centre of which faintly-staining threads of tissue lie.

As in Case 5, dead cells can be seen invaded by nuclei. In cortex, cord and ganglia the vessels are more distended with blood corpuscles than in the other cases.

Medullated Fibres of Spinal Cord.

In transverse sections, stained by *Wolter's method*, there is a very noticeable light staining of the crossed pyramidal tracts, which merges slightly into the posterior part of the ascending antero-lateral column, and also into the lateral cerebellar tract of both sides. The posterior columns present the same appearance, but in the cervical region the diminution of affinity for the stain is confined to the fibres in the postero-internal tract; in the lumbar enlargement the entire posterior region stains with less intensity than normal. On microscopic examination the myelin change is very evident—much more so than in any previous case—and in the lightly-stained regions one sees that the well-stained fibres are greatly in the minority. The ring formed by affected sheaths is a very thin one, stains faintly, and may be incomplete.

On account of the atrophy of so many tubes, those which are normal stand out with great distinctness.

The *Marchi method* shows many more fibres to be affected than in the other cases. Black dots are found in all the tracts, but there is a marked increase in numbers in the crossed pyramidal tracts, posterior columns, and in the direct lateral cerebellar.

In the dorsal and lumbar regions, the number of degenerated fibres in the crossed pyramidal tracts is greater than high up the cord, and the tract becomes more sharply marked o from the other columns.

In the lumbar region this is very well shown. There some degeneration in the posterior roots just before they ent the cord, and also some in Lissauer's tract.

In longitudinal sections the number of degenerated fibres is found to greatly exceed that observed in the previous cases, the rows of black droplets being very numerous (see photograph 11).

Combined Marchi and safranin method.—In this case very many tubes are affected, and large portions of myelin are completely atrophied, leaving the axis-cylinder quite denuded. The degree of degeneration is not so marked in some sheaths. There may be a slight diminution of affinity for the stain seen at intervals along the course of the fibre, and where bulging of the sheath has taken place the axis-cylinder commonly shows distinct fusiform swellings with regular outlines, but may still stain red. In those myelin dilatations there may be great tortuosity of the axis-cylinder.

As the myelin atrophies it tends to assume a pale violet colour, and the atrophy is patchy, picking out small spots or long segments, leaving well-stained, presumably healthy segments between.

In the vicinity of a node of Ranvier—which one rarely obtains a view of in sections, but which none the less can be seen to exist as a definite structure—this pale violet staining of the atrophied myelin is sometimes shown extremely well. The extremity of one node may stain quite normally, but on the other side of the constriction the myelin is thin, and vacuolated for some little distance, and is coloured a pale violet tint; the axis-cylinder is faintly violet also, and at some points unstained. Such pallor and atrophy may affect the nerve-sheath for a considerable distance, and many small vacuoles may be present. There may even be complete atrophy, leaving the axis-cylinder quite bare at some points, and here it stains very faintly violet, and shows fusiform swellings.

Pale violet-staining globules are seen arranged often in rows, representing the once healthy medullary tube, and at times one finds a row of red globules, the myelin between which has degenerated, and evidently been absorbed.

In the centre of these globules one frequently sees a spot which stains black with the osmic acid, the black patch showing up distinctly in contradistinction to the red-stained myelin which urrounds it.

Many droplets of this nature are met with in a more advanced ge of degeneration, where the patch of Marchi degeneration upies almost the entire globule, a very faint rim of myelin urrounding the black more central portion.

In the fusiform swellings of the axis-cylinder above mentioned, the centre may be much paler than the peripheral portion, an appearance which has been referred to previously.

Résumé of the appearances met with in the nerve-cells :—

Case 1.—In the cerebral cortex, and in the cord, one finds some cells showing a very slight degree of fragmentary change affecting the edge of the chromophile bodies generally throughout the cell, and others showing a typical central chromatolysis. In the cortex the nucleus of the small pyramidal cells stains very deeply and diffusely. There are a few cells in the grey matter of the cord which colour intensely blue and appear homogeneous. In the posterior root ganglia many cells show a central chromatolysis, and homogeneous atrophy of the nucleus is present in some instances. Vacuolation of the cells in this situation is not uncommon, when the chromatolysis is complete. Cells showing complete chromatolysis are present in the cord and cortex also.

Case 2.—In this case the nerve-cell degenerations are of the same types as given above, with two exceptions, viz., the nucleus of the small pyramidal cells of the cortex does not stain deeply and diffusely, and the deep blue homogeneous colour seen in a few cells of the cord in Case 1 has not been observed here.

Case 3.—The pigmentation of the nerve-cells in cortex, cord, and posterior root ganglia is in excess of the quantity found in Cases 1 and 2, but the hyperpigmentation does not exceed the physiological increase which one expects to find in a subject of 62 years of age.

The types of chromatolysis are the same as those given above. The nucleus of the small pyramidal cells stains deeply and diffusely, and in the posterior root ganglia also homogeneous atrophy of the nucleus is found, and is also present in cells which stain very deeply and have a homogeneous appearance throughout.

No deeply-stained homogeneous cells were observed [illegible] the cord of this case.

Case 4.—There is in this case a dissolution of the chromophile material in the cortical nerve-cells, and in the body of the cell a faintly-stained network can be perceived. The nucleolus is vacuolated.

In the spinal cord the types of chromatolysis are precisely of the same nature as in the first three cases, but of greater severity, as is indicated by the vacuolation found in the cell-body.

Case 5.—The cortical changes in this case are nearly the same as found in Case 4. In the cell-body one frequently finds vacuolation in addition to dissolution of the chromophile substance, and one meets with a very few large pyramidal cells in which there is no dissolution, but a slight fragmentation of the chromophile bodies.

In the spinal cord the changes are similar to those found in the preceding case, with the exception of vacuolation, but there are a few cells which show peripheral chromatolysis.

The changes in the posterior root ganglion cells are much more severe than in the first three cases.

Case 6.—Here one finds, in the cerebral cortex, dissolution of the chromophile bodies, a network in the cell, homogeneous atrophy of the nucleus in some cells, and vacuolation of both cell-body and nucleolus in others. In the cord there are a few cells with broken-up chromophile bodies, but the great majority show the same dissolution of chromophile material met with in the cortex cerebri. Some nerve-cell nuclei are in a state of homogeneous atrophy.

In the posterior root ganglia the greatest degree of change yet observed in those structures is found to exist. The chromophile substance is almost entirely dissolved away in the majority of the cells.

Some cells stain with great intensity, and homogeneous atrophy of the nucleus is always present in them.

Vacuolation of the cell-body is frequent.

Deeply-stained cells, with the nucleus in a condition of omogeneous atrophy, have been seen in the cortex also.

RÉSUMÉ OF CHANGES IN THE MEDULLATED FIBRES.

In all the cases the distribution of the degeneration and the form which it assumes are identically the same, and any difference in degree is very small, with the exception of Case 6.

In revising these morbid changes shortly, we find that:—(1) In transverse sections stained by Wolter's method, the crossed pyramidal tracts and the posterior columns possess less affinity for the stain than the tracts in the other regions of the cord. (2) Fibres yielding the Marchi reaction are found scattered in these columns, and to a less extent in other tracts also. The degeneration of the pyramidal tracts is much more intense in Case 6 than in the other cases, and is there most sharply defined in the lumbar region. (3) By the combined Marchi and safranin staining, two varieties of myelin alteration can be noted.

On some of the sheaths there are small round or oval points which stain black with the osmic acid, and around these points the myelin may be little altered. One or two of these black dots frequently coalesce to form a larger droplet. Sometimes, where the myelin has been broken up into round or oval globules, the centre of some of these may be stained black, while the peripheral part is stained partially by the safranin.

A form of degeneration differing in appearance from the above is met with, and consists in the atrophy and absorption of the myelin, leaving the axis-cylinder denuded partially or completely. Small and large segments of the sheath are affected, and portions on either side may show no apparent alteration. In this atrophic process there are to be noted the loss of staining reaction of the sheath, thinning and vacuolation often ending in complete atrophy along the parts affected, leaving the axis-cylinder bare.

Owing to an absorptive process having been superadded to the atrophic one in a complete atrophy of this nature, nothing is left to represent the once healthy myelin, so that this form of degeneration can be distinguished from th which ends in scattered globules or chains of droplets showing the Marchi reaction.

The axis-cylinder undergoes degeneration as well, a attention has already been drawn to such changes as impaired staining reaction, tortuosity, fusiform swellings, flattening, and in some instances thinning.

Actual rupture is an exceedingly rare occurrence, and has only been observed in one of the six cases.

From what has preceded, it will be seen that tissues from the central nervous system have alone been preserved and examined. The changes in the peripheral nerves, the liver, intestines and kidneys, have not been studied.

Since the commencement of this research, the importance of retaining portions of these organs for examination in order to form a more complete work has received due attention, and in all cases of acute insanity which have been met with since the above series was begun, this oversight has been rectified in view of future publications on the subject.

That an examination of all the organs of the body—and even of the blood itself—is of the utmost importance, is forced upon one's attention by a perusal of the recent literature upon acute mental troubles.

In two cases of insanity following influenza, Camia (2) found fatty degeneration of the liver and kidneys. In a more recent publication on the changes found in the nervous system in acute confusional insanity, the same author—in addition to the nerve-cell and fibre changes—describes the following definite alterations.

Kidneys.—Fat droplets in the cells of the convoluted tubules and of the glomeruli; the vessels between the tubules much dilated and congested. In the tubules dead cells are found, and in the loops of Henle the protoplasm of the epithelial cells is broken up and pale.

Liver.—Fatty degeneration of the hepatic cells and dilatation of the central vein of the lobule. Fatty degeneration of the muscular fibres of the heart has also been seen.

Zonder (39), in experimental subacute poisoning by aluminium, found definite changes in the nervous system, but in addition the kidneys and liver showed distinct lesions. In the former he found cloudy swelling, and in many tances destruction and shedding of the epithelium of the nvoluted tubules, which at times were full of these dis- ntegrated structures, and in the mass so formed fat droplets could be seen.

In the loops of Henle there were large, deeply-staining particles, also destruction of epithelial cells. In the straight tubules, and in the glomeruli, the nuclei were swollen, and many showed karyokinetic figures.

The connective tissue nuclei were proliferated.

In the liver he found extravasation of leucocytes around the vessels, and many leucocytes scattered between the liver cells; near the small arterioles were small hæmorrhages.

According to Camia, the changes found in his cases are to be regarded as the result of an intoxication, but at the same time he contends that there is evidence to show that the stasis in the vessels of the liver and kidneys has played a part in the causation of the degeneration.

Turner[1] also explains in this way the fatty degeneration of the liver found by him in cases of acute delirium.

The six cases under consideration can be divided into three groups, according to the character of the nerve-cell change met with, and also according to the severity of the alterations produced.

In the first three cases the changes, with slight exceptions, are very similar in appearance, the most predominant feature common to all being the central chromatolysis found in the cells of the cortex, anterior cornua of the cord, and in the posterior spinal root ganglia.

This central chromatolysis is found to be associated with excentricity of the nucleus when the nerve-cell reaction has reached a fairly advanced stage.

In Cases 4 and 5 the chromatolysis found in the cortex is of a more acute type, and if one excepts the limited number of large pyramidal cells in the fifth case, in which there is not a dissolution but a slight fragmentation of the Nissl bodies, then the appearances will be seen to be precisely similar and the degree of the lesion almost equal in each.

In this group the type of chromophile disintegration i the nerve-cells of the cord is identical with that found the first group, but the greater amount of damage inflict on the nerve-cells is shown by the presence of vacuolation in them in the cord of Case 4, and by the more acute chromatolysis in the cells of the posterior root ganglia of Case 5.

Case 6 stands out markedly from all the other cases on account of the grave nerve-cell degeneration which is found throughout the entire central nervous system. Here, too, the fibre reaction is greatly in excess of that found in the previous cases.

Unlike Cases 4 and 5, where the cortical changes are more severe than in the centres lower down, we find that with the exception of a few cells in the cord, in which fragmentary changes are present, the type of cell change met with is the same in all regions.

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[1] J. Turner. "Acute Delirious Mania." *B. M. J.*, No. 2073, 1900.

Let us now look at the various forms of nerve-cell reaction, and see in how much they agree with the changes found by others in cases of a similar nature, and in recent experimental work.

The slight fragmentary change which affects the edges only of the chromophile elements generally throughout the cell has been observed in Cases 1, 2, and 3, in some of the large pyramidal cells of the cortex, and in the large multipolar cells of the anterior cornua.

In Cases 4 and 5 this change is found only in the latter situation. Such a slight degree of alteration in the nerve-cell occurs with much less frequency than the others to be described, but is none the less of considerable importance as pointing to the greater stability of the large cells, rich in well-formed chromophile material.

Camia (4) has found such changes in acute mental confusion and in insanity following influenza, in both cortical giant cells and in anterior cornual cells.

This same author has found a similar degree of alteration, in the same situations, in certain experimental poisonings 3), and notes the fact that the smaller varieties of nerve-ells show in many instances a more profound degree of eration than the larger ones.

But the type of nerve-cell change which one finds most frequently in all the cases cited above is a central chromatolysis, which is seen in various stages of its development, and which varies from a slight degree, limited almost entirely to the area in the immediate vicinity of the nucleus, to a more profound alteration, in which normal chromophile bodies are only found at the periphery and in the protoplasmic processes. At this stage there is displacement of the nucleus outwards.

Central chromatolysis has been found in the cortex, cord, and posterior root ganglion cells in the first three cases, in the cord of Case 4, and in the cord and posterior root ganglia of Case 5.

Only in certain cells of the posterior root ganglia is the change really identical in appearance with that met in the cortex and cord. I refer to the medium-sized cells, in which the chromophile elements are large.

Various writers within recent times have met with and described this form of nerve-cell alteration in different forms of mental derangement.

Ballet and Faure (1), in cases of mental confusion, found the cortical giant cells swollen, and affected by a central chromatolysis with excentricity of the nucleus. In one case, which also presented marked symptoms of polineuritis, a similar type of alteration was present in the cord.

Camia, in confusional insanity, found the same change in the cortex, cord, and to a less extent in the posterior root ganglion cells.

Meyer (22) figures a giant cell showing the same condition.

Trömner (35) describes a similar appearance in the spinal ganglion cells of a case of delirium tremens, as also does Turner (37) in the cortex of cases of dementia, melancholia, and of delirium.

But although found present in the above mental states, there are other conditions in which such an alteration as the above has been found. For example, Marinesco (17) found the same change to occur in the cerebral cortex secondary to lesions of the internal capsule; and in a case of pellagrou insanity, described by Righetti (28), in which the spinal roo were affected, the cells in the anterior horns of the cord, and to a less extent the cells of the posterior root ganglia, showed well-marked central chromatolysis with peripheral displacement of the nucleus.

Again, Schüpfer (32), in a case of tetanus with left facial paralysis, found central chromatolysis in the cells of the cortex, and also in the left facial nucleus.

In poisonings, experimental and otherwise, the same type of reaction has been seen, *e.g.*, by Nichols (24) in typhoid fever, and after infection of rabbits with the typhoid bacillus; by Rossi (30) in poisoning with phosphorus; and by Tschernischeff (36), as a result of grave gastro-intestinal symptoms following fish-poisoning. In the last-mentioned author's cases, however, peripheral and diffuse chromatolysis was also noted, and also the presence of vacuoles in the cells.

It will be remembered that in the cortex of Cases 4 and

5 and in the entire central nervous system of Case 6 there was a much greater degree of cell alteration than was seen in the first group, and the appearances suggest that instead of a fragmentary change, as is found in the central chromatolysis above described, one has here to deal with a process of dissolution of the chromophile material.

The remarkable way in which the cell stains in a diffuse manner throughout the body and processes, and the almost total absence of chromophile material, indicate the profound degree to which these cells are affected. There are indications in some cells, however, which would lead one to the belief that the process of dissolution has commenced in the central parts of the cell, for when any chromophile bodies persist they are found around the periphery and in the processes.

Associated with this process of dissolution one sometimes finds vacuolation of the cell-body and also of the nucleolus, conditions which are commonly met with in [illegible]ertain toxæmias.

[illegible]addi (11), in examining the nervous system of animals [illegible]ted with hydrophobia, found that the cells stained in a [illegible]use homogeneous manner, and that vacuolation of the [illegible]l-protoplasm was present.

De Buck and De Moör (12), in experimental tetanus, [illegible]escribed a rapid dissolution of the chromophile substance, causing intense colouration of the cells.

In some cells they found a faint protoplasmic reticulum.

Tschernischeff (36) has found a similar change in some of the cells in the cases of fish-poisoning already referred to.

In other disturbances of the nervous system vacuolation is frequently found:—By Ciaglinski (8) in the cells of the anterior cornua in death from acute tuberculosis, and in the posterior root ganglion cells of a fatal case of diabetes; by De Buck and De Moor (13) as a result of induced acute anæmia (in some of the cells vacuolation of the nucleolus was present); and by Nartowski (23) in rabbits infected with the diphtheria toxine. Similar conditions have been described by Soukhanoff (33) and Zonder (39) in experimental poisonings with arsenic and aluminium.

From the above results it is evident that vacuolation in the cell-body is liable to occur secondary to the entrance of toxines or poisons into the system, and also as a result of interference with the blood supply, and the vacuoles are usually found associated with grave alterations in the chromophile material, such as advanced chromatolysis, or, as we have seen, with chromophile dissolution.

Vacuolation of the nucleolus is much more rarely found, and in the present series was only observed in the last three cases.

If one refers to the description of the posterior root ganglion cells of Case 3, and the cortical and spinal root ganglion cells of Case 6, a rare type of degeneration will be found, which is clearly quite different from either a true chromatolysis or a chromophile dissolution. The cells which come under this type are recognised by the deep, homogeneous manner in which the cytoplasm stains, and also by the presence of homogeneous degeneration of the nucleus associated with the cytoplasmic change. This inten homogeneous colouration of the cell has been four Marinesco (19) in acute encephalitis, and was first call him "partial or superficial coagulation with corpusc formation," on account of the fact that some parts of t periphery of the degenerated cell were detached, and l closely applied to its edge. In a later publication (20), h alludes to the same coagulation process, or, as he sometimes terms it, coagulation necrosis, and admits that the centre of the cell may be affected, and in addition he has found the nucleus in a condition of homogeneous degeneration.

Homogeneous degeneration, or atrophy of the nucleus was first described by Sarbó (29), and its development can be divided into two stages. In the first stage the nucleus is stained very deeply and diffusely, the nuclear network is obscured, but the nucleolus remains visible.

The second stage is characterised by the intense colour already noted, and in addition the nucleus is now greatly reduced in size and its contour is very irregular.

Trömner (35), in some spinal cells in delirium tremens, has found similar very deeply-staining cells, in which he has seen a thick felted network and homogeneous atrophy of the nucleus.

Schukowsky (3), in acute delirium, has found cells which present exactly the same appearance, and Guizzetti (14) has described them also in a fatal case of chorea in which there was vegetative endocarditis with septicæmia, and staphylococci were present in the vessels of the brain.

But even in cells in which the above cytoplasmic change is not found one may see both early and late phases of this homogeneous atrophy of the nucleus.

In the small pyramidal cells and in the spinal root ganglion cells of Case 1, in the posterior root ganglion cells of Case 2, and in the small pyramidal cells of Case 3, this nuclear alteration has already been noted, and it is remarkable how often it has been found present in cells whose chromophile material shows little alteration.

It is very difficult to account for this early nuclear atrophic change in cells otherwise practically normal in appearance, for it is one's experience to find that with interference of the nerve-cell function the chromophile rial shows changes before any are noticeable in the eus, and alterations in the latter structure are shown a progressive pallor. But in homogeneous atrophy the posite is the case, and the nucleus is the first part of the ll to suffer.

De Buck and De Moor (13) have found after occlusion of the abdominal aorta that homogeneous atrophy of the nucleus occurs early in the nerve-cell degeneration brought about by the acute anæmia, and Righetti (27) has noted a similar change from the same cause.

Amongst others who have drawn attention to this nuclear homogeneity with atrophy in toxic conditions are Nartowsky (23) and Shüpfer (32); while Rossi (30) and Soukhanoff (33), in metallic poisonings, have found the nucleus more highly coloured than usual, an appearance which may be interpreted as an early stage of homogeneity.

Although our knowledge of the conditions which bring about such an early and profound nuclear alteration is very deficient, yet, whatever may be the cause of it, there can be little doubt that the cell in which such an early nuclear alteration occurs can never recover, for it is generally admitted that the integrity of the nucleus is necessary for the life or regeneration of the chromophile material. Once a nucleus becomes affected by this homogeneous atrophic process, not even the removal of the exciting cause of the degeneration can lead to restoration of the nuclear function.

The same, naturally, can be said of the cells which are in a state of coagulation necrosis, and as homogeneous atrophy of the nucleus has always been found present here, perhaps one is not wrong in assuming that the said atrophic nuclear change is the precursor of the coagulative necrosis in the nerve-cell.

In some of the nerve-cells of Cases 4, 5 and 6 a network can be seen. This is rather faint in Cases 4 and 5, but in the last it is quite distinct. The network is composed of meshes of equal size, pervades the whole cell-body, and extends for a little distance into the processes. From the characteristics described, this seems to be identical with the fine network of Donaggio (29).

The alterations of the myelin-sheath and axis-cylin[illegible] in the cord have been seen to be as constant a feature [illegible] all the cases as the changes in the nerve-cells, and [illegible] found to vary very little in intensity in the first five, but [illegible] the sixth the degeneration of myelin is of a much more seve[illegible] character. The distribution of the degenerated fibres has been studied in transverse sections, but in order to examine into the nature of the myelin and axis-cylinder change it has been necessary to study them in longitudinal section, and to use a stain which would allow of both being examined at the same time. Safranin has answered the purpose admirably, especially after tissues had passed through the Marchi process.

Alterations of a similar nature to those described under each case have been observed in certain mental affections and in certain toxic poisonings.

Camia (4), in acute confusional insanity, has described in detail the changes found in the white matter of the cord, but here one can only give briefly his results and views.

By the Marchi method he found a slight degree of degeneration in the pyramidal tracts, which was more marked in the dorsal region. In sections stained by the Weigert method these tracts were more lightly stained and the volume of the individual fibres diminished. The fibres nearest the grey matter were more affected. In the dorsal cord he found small areas in which, with high magnification, the myelin was seen to be quite destroyed, leaving the axis-cylinders bare.

Destruction of myelin-sheaths has been seen by Schukowsky (31) and by Carrier (5) in acute delirium, and in the same condition Cristiani (9) found in the central nervous system and in the cranial and peripheral nerves a degeneration of the myelin, which according to him was of a primary nature. Primary degeneration of the sheath has also been described by Mager (21) in acute myelitis. Nichols, in his experiments already referred to, in addition to the nerve-cell changes, has drawn attention to a parenchymatous degeneration of the peripheral nerves; and [illegible]en and Laitinen (15), after injecting cultures of [illegible]ptococci into the sciatic nerve of an animal, were able to [illegible]e diffuse alterations, ending in granular fragmentation of [illegible]e medullary tube.

The term "primary atrophy" of the myelin-sheath has been given by Vassale (38) to a special form of degeneration in which the appearances are quite different from those found in degeneration of the fibre as a consequence of its destruction, or breach of its continuity with its trophic centre.

Briefly, the features which characterise the primary degeneration of Vassale are loss of staining reaction, thinning and slow disappearance of the myelin, occurring in a scattered manner along the sheath, and until complete demyelinisation of the axis-cylinder results. According to this author, the degeneration is toxic in origin, and may be caused by either exogenous or endogenous poisons, and he accentuates, as an important differential sign between primary and secondary degeneration, the fact that in the former the axis-cylinder persists for a great length of time, although showing slight alterations; whereas, as is well known, there is grave destruction of both the myelin-sheath and axis-cylinder in the secondary degenerations.

Righetti (28), in the spinal roots of a case of pellagrous insanity, has described and figured appearances which he terms primary atrophy of the fibres as shown by swelling, diminished staining, and thinning of the myelin covering, accompanied by swelling and pallor of the axis-cylinder.

In the six cases under discussion, slight and more advanced modifications of staining reaction are common appearances in the axis-cylinder, and both thinning and fusiform swellings have been noted.

But actual rupture has been very infrequently observed, and no appearances resembling the fibrillation or disintegrative-changes such as Thomas (34) has figured as occurring in multiple sclerosis have been met with.

Taking into consideration, then, the patchy atrophic character of the myelin changes, and the comparatively slight affection of the axis-cylinder, it is evident we have here a typical primary degeneration.

But while one can definitely affirm that the m[illegible] atrophies seen by safranin staining are primary in origin[illegible] finds it difficult to account for the Marchi degenera[illegible] which we have seen in the crossed pyramidal and poster[illegible] columns. Turner (37) and Camia have noticed the Marc[illegible] degeneration in the pyramidal columns in acute menta[illegible] affections, while Marinesco[1] has found a similar affection of the same regions; and Camia also notes that many experimenters have described degeneration in the pyramidal columns brought about by the action of toxic substances which attack the fibres in these regions primarily.

But in all the six cases we have found that the posterior columns show fibres yielding the Marchi reaction as well as the pyramidal, and this association of posterior and lateral column degeneration has already been noted by Donaggio[2] ("nelle psiconevrosi acute"), and is, according to him, to be ascribed to a toxic origin.

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[1] Marinesco: "Lésions des Centres Nerveux dans la Pellagra" (*Comptes Rendus de la Soc. de Biol.*, No. 35, 1899).

[2] Donaggio: *Rivista Sperimentale de Freniatria*, Fasc. IV., 1897.

It is a curious coincidence that the pyramidal and posterior tracts should show a preponderance of fibres showing the Marchi reaction, and the question before us now is whether this Marchi degeneration is of a primary or secondary nature, and if primary, why should not other regions of the cord show an equal amount of it.

Of course it must not be forgotten that, by the combined Marchi and safranin stain, definite primary atrophies and typical rows of Marchi degeneration have been seen side by side in the same section, taken from a longitudinal slice along the middle of the cord.

But, as Camia points out, there is now sufficient evidence to show us that the pyramidal and posterior columns possess less resistive power to the action of toxic substances, and he is of opinion that the degeneration in these regions is primary, and due to the same cause as the alterations found in the nerve-cells of his case.

To account for the presence of Marchi degeneration, however, he is inclined to lay great stress upon the prolifera- [illegible] in the cord of his case of confusional [illegible] liferation may [illegible] stances, while the large majority of them are in a state of acute chromatolysis, a condition from which they can recover granted that the causative agent is withdrawn.

Further, although Vassale holds that Marchi droplets are not found in typical primary degeneration on account of the slow atrophic nature of the process, yet there are certain appearances, especially in Case 6, which can be advanced against this view, for we have seen small patches of Marchi reaction, situated in segments of the sheath, which still stained with safranin, and in other parts of the same sheath the typical atrophic primary degeneration was present.

It is thus possible that some parts of the myelin succumb to the local action of the toxine more quickly than other portions, and so give rise to changes which differ considerably in appearance, but which are nevertheless caused by the same factor.

It is certainly difficult to believe that in Cases 1 and 2, which it will be remembered ran a course of short duration, there was time for the neuroglia to proliferate to such an extent as to cut off the axis-cylinders [illegible] and so give rise [illegible] intoxication. There is no doubt that the changes in the myelin-sheaths and axis-cylinders are primary, and the same can be said of the nerve-cell alterations, although some might not be inclined to accept the view that the central chromatolysis with peripheral displacement of the nucleus is so.

This latter change is similar in appearance to the alterations found in the nerve-cell as a result of the division of its axis-cylinder, and has been described in the work of Marinesco, Lugaro, Van Gehuchten, and many others (29); but although similar in appearance, we are not justified in concluding that the presence of central chromatolysis in our acute cases of insanity is to be accounted for by injury of the conducting fibre.

In a general intoxication it is inconceivable that such a highly differentiated and delicate structure as the nerve-cell could possibly be later in reacting to the toxine than the other nervous tissue, for we must bear in mind the fact that [illegible] nerve-cell has been shown to be provided with cana- [illegible] which permeate it and distribute the nutrient fluids [illegible] the blood throughout the cytoplasm, so that the cell [illegible]t react readily to all modifications in the constitution [illegible]the circulating media. The fact that the chromatolysis [illegible]mmences in the central parts of the cell can be explained [illegible]atisfactorily on developmental grounds. Marinesco (18), in his studies on the involution and evolution of the nerve-cell, has shown that the chromophile elements in the centre are the last to be developed, and one is inclined to agree with him when he says that their stability is less than that of those at the periphery of the cell, which are the first to be developed.

It is obvious, then, that in a general intoxication such as we are at present discussing, these central elements must present less resistance to the toxic agent, and succumb more quickly, thus giving an appearance like that of the *reaction à distance*.

Moreover, in all the six cases described, only slight changes have been seen in the axis-cylinders, so that on anatomical and developmental grounds, together with the absence of sufficient alteration in the fibre to cause secondary reaction in the cell, we must consider that even the central chromatolysis is due to the direct effect of a toxine acting on the cell itself. This at present is the view which most authors adopt who have worked at the subject.

Although the pathological changes found in the acute insanities point clearly to an acute general intoxication, in which the toxic substances attack the nervous system and all the other tissues of the body, yet we are still far from having a clear idea of the source of this intoxication.

The *rôle* of toxines in the production of nervous disorders now rightly receives a considerable share of attention, for sufficient evidence has been put forward of late years to show that there is a close connection between toxic conditions of the blood and affections of the nervous system.

A concise classification of the various sources of toxic infection which one has to consider in studying nervous diseases, is given in "Robertson's Textbook of Patholo[illegible] relation to Mental Diseases."

These are as follows:—(1) Exogenous poisons, [illegible] alcohol, cocaine, morphia, &c. (2) Poisons formed wi[illegible] the body in the course of various infective and non-infect[illegible] diseases, *e.g.*, influenza, syphilis, rheumatism. (3) Poison[illegible] generated within the body owing to disorders of metabolism—auto-intoxication, *e.g.*, Bright's disease, myxœdema, diabetes, &c. In this group are placed the toxines which are developed as a result of bad hygienic conditions, mental shock, or overstrain. (4) Poisons generated in the intestinal canal as a result of derangement of the digestive organs. When these toxines pass into the system, we have to deal with an auto-intoxication of gastro-intestinal origin. (5) Poisons developed by the action of organisms which have passed from the alimentary tract into the blood. This condition of infective toxæmia has been worked at by Bianchi and Piccinino, and more recently by Ceni, whose results are of the greatest interest, and will be referred to later.

D'Abundo and Agostini, in the *Rivista Sperimentale di Freniatria*, fasciculus iv., 1900, have entered fully into the question of the *rôle* of intoxications and infections in the pathogenesis of nervous disorders, and the accumulation of facts given in their conjoint paper is quite sufficient to show the importance of these factors as causative agents.

In discussing the source of the intoxication, these authors draw attention to certain facts in order to demonstrate to what an extent the individual is constantly exposed to the risk of infection through the mucosæ, especially through that of the intestinal tract.

The cavities of the body are normally full of organisms, and the mucosa itself is one of the natural barriers which offer a constant resistance to the entrance of either the toxines or the organisms themselves.

Now, according to D'Abundo and Agostini, there are certain mental conditions which are known to so modify phagocytic action, and therefore resistive power, that the line of defence—as they call it—is weakened. Such conditions are mental shock, fright or worry, and any other con[illegible]tion which brings about a lowering of tone of the nervous [illegible]em, which naturally reacts upon the tissues of the body [illegible]erally, for the integrity of the former is, as we know, [illegible]essary for the proper carrying on of the function of the [illegible]ter.

If we look back to the third group of poisons, we see that mental shock, overstrain, and bad hygienic conditions can induce a condition of auto-intoxication. The toxines so produced ought to be neutralised by the secretions of the protecting organs of the body, *e.g.*, the liver, pancreas, kidneys, and lymphatic glands; but if through defective function of these organs the process of neutralisation is not sufficiently carried out, then an accumulation of toxines takes place in the organism, which will immediately react on the nervous system, to its further detriment.

Now, according to D'Abundo and Agostini, this induced primary intoxication paves the way for the production of secondary intoxications, which may either be caused by chemical modifications in the viscera due to disturbance of nervous influence, or by the circulation of the primary toxine itself in the blood.

But the presence of a primary intoxication may so lower the resistive power that micro-organisms may gain access to the blood-stream, and so induce an infective condition which complicates greatly the nervous symptoms.

The work of Ceni (6) in this connection is of so much importance that it seems of advantage to note some of his results and his conclusions.

In studying cases of delirium he has examined the blood in order to ascertain at what period of the disease micro-organisms were present.

Prior to his researches Bianchi and Piccinino found and described a special bacillus in the blood and meninges of cases of acute delirious mania, and they held the view that, given heredity and poverty of the system, micro-organisms could attack the individual and induce delirium.

But Ceni differs from these authors, and holds that their theory may be right only for cases in which their special bacillus is found, because he himself has frequently observed the common micro-organisms to be present in the blood [illegible] epileptics not suffering from delirium.

Ceni, in his bacteriological examinations, has found t[illegible] in the early phases of delirium no organisms are present [illegible] the blood; but as soon as the excitement is accompanied b[illegible] fever, then organisms make their appearance. With th[illegible] elevation of temperature the symptoms are more grave, and death rapidly follows.

The organisms which he found in one case were the staphylococcus pyogenes aureus, and a short, slightly mobile bacillus which had all the characteristics of the bacterium coli; in a second case the blood contained the streptococcus pyogenes and the micrococcus tetragonus.

The bacterium coli was only found in the blood immediately before death.

According to Ceni, this late infection is not the cause of the mental symptoms, but it nevertheless constitutes a very grave complication. He thinks that the nerve-cell changes reduce the alkalinity of the blood, alter the bactericide and phagocytic functions of the blood and tissues, so that there is an invasion later by the common germs which normally occupy the the cavities of the body.

In a later publication Ceni (7) gives the result of his examination of forty-six cases of various psychopathic forms, including acute delirium, severe mania, uræmic convulsions, maniacal attacks in general paralysis, prolonged status epilepticus, &c.

In fourteen cases, during the acute stage, he found in the blood streptococci, staphylococci, pneumococci, micrococcus tetragonus, bacillus coli, and bacillus pyocyaneus.

He has concluded that these organisms never appear in the blood at the beginning of an attack, but shortly after an exacerbation, and their appearance is accompanied by febrile change.

Generally, the infection is determined by a single form of organism, but when death is approaching, then mixed forms are found in the blood.

These investigations of Ceni are worthy of the highest commendation, for they definitely prove that the entrance of organisms into the general circulation influences the course of mental disorders markedly for the worse, especially if the ection is bacillary.

At the same time, his postulate that there must be some nctional or organic disorder of the nervous system first resent must never be forgotten, for the complicated processes nvolved in this primary disorder form the crux of the whole question of the causation of insanity.

The hereditary taint is universally admitted to be the greatest of predisposing factors, and there can be no doubt that auses such as mental shock, worry, overstrain and privation [illegible] one the subject of hereditary weakness, [illegible]ation, and so precipitate acute insanity which one may meet, from a neuropathological, physiochemical, and pathochemical standpoint, that our knowledge of this subject will advance.

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UNIRADICULAR PALSIES OF THE BRACHIAL PLEXUS.

BY E. FARQUHAR BUZZARD, M.B., M.R.C.P.,

Assistant Physician to the Belgrave Hospital for Children and Registrar to the National Hospital for the Paralysed and Epileptic.

The object of this paper is (1) to place on record six cases in which the symptoms pointed to a lesion of one of the spinal nerves forming the brachial plexus, (2) to discuss the sensory and motor phenomena produced by such a condition, and (3) to consider the anatomical site and pathological basis of the morbid process concerned.

I gratefully acknowledge my indebtedness to Sir W. wers, Dr. Ormerod, Dr. Beevor, and Dr. Taylor, for their d permission to make use of cases under their care at the ational Hospital, as well as to Dr. Sworder and Dr. Collier r notes on a patient whom they saw in private practice.

The diseased condition had an acute onset in the first three cases described.

Case 1.—J. J. P., a young man 25 years of age, was admitted to the National Hospital, under the care of Sir W. Gowers, on November 10, 1901. About a year previously, whilst acting as orderly in the R.A.M.C. in South Africa, he had a fall from a horse, which caused him no serious inconvenience or discomfort. Six weeks later he was attacked by acute pain in the right side of the neck and shoulder, which lasted about a fortnight, and which was accompanied by rapid wasting of the muscles in the shoulder girdle region. The loss of power and wasting reached their maximum in a month or six weeks, and then remained stationary up to the time of his admission into the National Hospital.

In the meantime he had been treated in South Africa and at the Nottingham General Infirmary. There had been no return of pain, and the patient complained only of inability to raise the arm at the shoulder.

On examination, the man, though slightly pale, presented the appearance of good general health and muscular development. The signs of disease consisted in atrophy and paralysis of the right supraspinatus, infraspinatus, deltoid and teres minor muscles, and in disturbance of sensation over an area roughly covering the deltoid muscle (see figs. 1 and 2).

The atrophy in the spinati and teres minor muscles was extreme, and no response was obtained to faradic or galvanic currents; a few fibres of the deltoid responded to strong currents, whilst the greater part of the muscle was unresponsive. The right biceps was no larger, and perhaps a trifle weaker, than the left, but it reacted well to stimulation by electricity. No affection of the supinator longus or brachialis anticus could be detected, nor of the trapezius, rhomboids, serratus magnus, pectorales, or diaphragm. It was not possible to detect any defect in function in the subscapularis.

As regards sensation, the area depicted in fig. 1 was quite analgesic; touches were felt there, but seemed different, according to the patient, to touches elsewhere; heat and cold sensibility was very defective over the same part, and the man thought he recognised heat with more difficulty than cold. Elsewhere the neuro-muscular system was normal, and no signs of visc[illegible] disease could be detected. After some weeks of treatment [illegible] massage and galvanism, symptoms of improvement began to set [illegible] with regard to the deltoid; and at the end of February, 1902, th[illegible] muscle displayed very considerable voluntary power. A few fibr[illegible] of the infraspinatus again began to function under volitiona[illegible] stimuli, and the area of analgesia was almost gone. The patient left the National Hospital early in March with a useful limb and with improvement still taking place.

In this case no etiological factor could be obtained from the man's previous history, and it is extremely unlikely that the trauma mentioned had anything to do with the condition. It may be added, however, that at the time of onset he was working very hard on half rations of food. No fever was associated with the early days of the disease.

Case 2.[1]—A. O., a married woman, 40 years of age, came to the Hospital in February, 1901, and was treated as an out-patient under the care of Dr. Beevor. She came complaining of weakness in her right hand, and gave the following history.

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[1] This case was shown by the author at the Neurological Society in March, 1901.

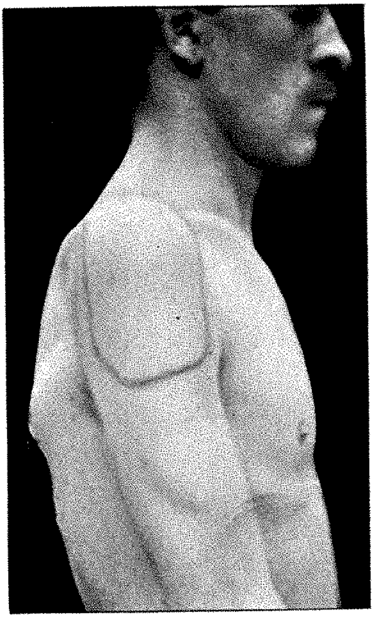

FIG. 1.

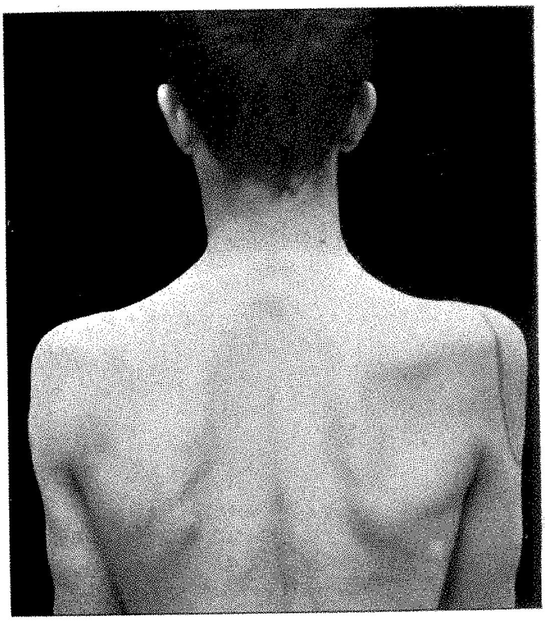

FIG. 2.

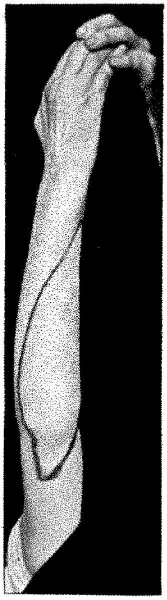

FIG. 3.

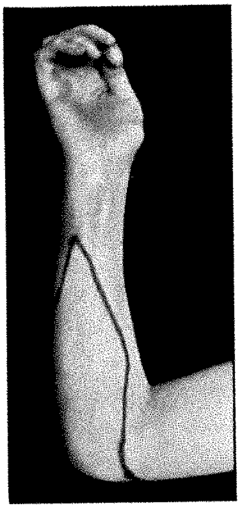

FIG. 4.

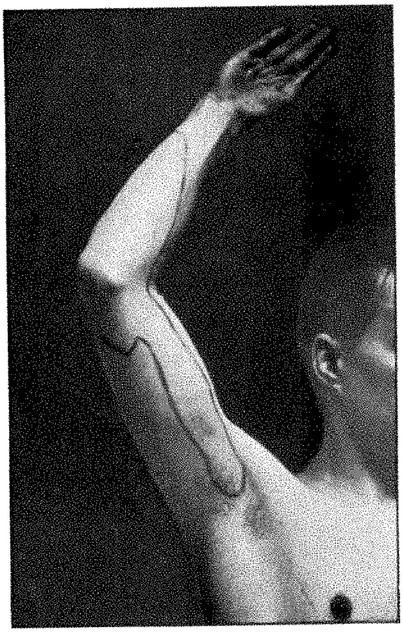

FIG. 8

Five years ago she was at Malta, and had an attack of Maltese fever. During convalescence she woke up one morning with pain shooting down the right arm from the neck and shoulder, and weakness of her right hand. The muscles of the latter slowly wasted, and have remained in a stationary condition ever since. The pain lasted a few days and then disappeared, to return from time to time for short periods. She was unaware of any numbness or loss of sensation.

On examination, there was found, in an otherwise perfectly healthy woman, marked atrophy of the muscles of the right thenar eminence, with partial atrophy and paresis of the interossei and long flexors of the fingers. At the same time an area of analgesia and thermanæsthesia, with slightly impaired sensibility to touch, on the inner surface of the forearm was detected. This area was somewhat oval in shape, and extended from a point just above the wrist to another just above the inner condyle of the humerus, the edges being fairly sharply defined (see figs. 3 and 4).

Electrical Reactions.—Practically no response to either current in thenar eminence, feeble contraction with faradism and galvanism in hypothenar muscles, interossei, and long flexors of the fingers, but no polar change and no qualitative change with the galvanic current.

The pupils and palpebral fissures were equal on the two sides. No improvement and no retrogression took place under treatment.

This patient was seen again after a long interval on June 6, 1902. The muscular wasting and sensory disturbance were in *statû quo.* The area of dissociated anæsthesia was tested by means of the cautery and ether spray (see Case 6), and the following results were obtained. The territory denoted in figs. 3 and 4 was insensitive to pin-pricks and to radiating heat, partially insensitive to cold vapour, and sensitive to tactile stimuli in a modified way (*i.e.*, the patient said they did not feel the same as elsewhere). At the same time I was struck with this fact: the fine point of a pin not only failed to give rise to painful sensations, but in most places failed to elicit tactile sensations. The cautery, placed in contact with the skin and raised to a moderate temperature, produced no sensation of heat nor any sensation but that of touch.

Case 3.—Mrs. W., aged 50, experienced sudden loss of power in left shoulder, with pain down the left side of the neck and shoulder, in June, 1900. This was followed, a few days later, by herpes, for which Dr. Sworder treated her. Recovery was slow, and in November, 1901, she was seen by Dr. Collier, who found atrophic palsy of left deltoid, supraspinatus and infraspinatus, with hardly any faradic response in any of those muscles. He also found some anæsthesia and analgesia of the fifth cervical root area, and the scars of herpes in the same region. There were adhesions in the shoulder joint, which were subsequently broken down, with the result that improvement rapidly took place, and when I saw her, early in this year, considerable voluntary power had returned and the sensory symptoms had practically cleared up. I learnt from her that she had had rheumatic fever when 19 years of age, and had suffered ever since from shortness of breath, faints, and cardiac pain. On examination there were well-marked signs of mitral stenosis. Unfortunately I have no accurate map of the anæsthesia or herpes distribution in this case; but in the present condition of our knowledge as to the significance of herpes, we may assume with a great degree of certainty that the lesion here was a vascular one, affecting the fifth cervical posterior root ganglion and spreading to the fibres of the anterior root at their junction with the posterior.[1]

The following cases presented a subacute or insidious onset, progressed for a short period, but had for some time been stationary. Under treatment some improvement has taken place in certain of them.

Case 4.[2]—E. C., a girl in domestic service, 19 years of age, came to the Hospital on October 23, 1901, complaining of weakness of the right hand. When twelve years old the patient had scarlet fever, and an attack of chorea a year later was followed by a second attack four years ago. About that time she began to notice some flattening of the right thenar eminence and a gradually progressive weakness of the right hand. Very little alteration had taken place recently, and there was no extension of the disease to other parts. The onset and course of the condition had been unassociated with pain.

On examination the girl was well nourished and healthy looking, but complained of being short of breath on exertion. There were no evident signs of cardiac disease. Pupils and palpebral fissures were equal on the two sides. There was great atrophy of the abductor and opponens pollicis, less marked atrophy and weakness of the adductores and flexor brevis pollicis, much loss of power and atrophy in the interossei, hypothenar muscles, and long flexors of the fingers; there was loss of faradic and galvanic excitability in proportion to the wasting. The fingers presented a tendency to the "claw" position. On the inner side of the forearm there was an area of analgesia and thermanæsthesia, with partial loss of tactile sensibility, corresponding very closely in shape and size to that seen in Case 2 (fig. 5). No other abnormalities of a sensory, motor, or reflex character were present. Considerable improvement in regard to the sensory disturbance and slight increase of motor power has been observed under treatment.

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[1] This was the diagnosis arrived at by Dr. Collier when he saw her in November, 1901.

[2] This case was shown by Dr. Beevor at the Neurological Society on October 31, 1901.

Case 5.—E. M., a married woman, 33 years of age, has been attending at Queen Square as an out-patient under Dr. Ormerod's care for some years. When 18 years of age she suffered severely from anæmia, and was in a hospital for three months with that complaint. Shortly afterwards she noticed that her right hand would often "go cold," and subsequently she observed wasting in that part. This wasting has gradually progressed until, at the present time, most of the intrinsic muscles of the hand are affected, whilst the fore and upper arm are free from marked atrophy or paresis. On testing the sensibility an area of analgesia and relative anæsthesia similar to that in Cases 2 and 4 is detected on the ulnar aspect of the forearm. There are no signs of disease elsewhere, and the pupils and palpebral fissures are equal.

The heart and other viscera are healthy. The patient is free from pain, although in the past there have been attacks of aching down the inner side of the right arm.

The following case differs from those which precede it in the fact that two spinal nerves, the first dorsal and the fifth cervical, have both been affected, the one severely, the other slightly.

Case 6.—K. P., a domestic servant, 28 years of age, came under Dr. Taylor's care on February 20, 1902. Six years previously she had influenza, and for four years subsequently she suffered from trouble with her stomach. Her symptoms consisted of vomiting, hæmatemesis, epigastric pain, amenorrhœa, shortness of breath and palpitation of the heart, and three years ago these troubles became so acute that she was treated in the Bristol Infirmary for four months. About two years ago she began to be conscious of clumsiness in her right hand, and found that she had difficulty in using her fingers, especially in cold weather. At the same time wasting of the thumb was noticed, and attacks of pain in the arm, which have recurred at intervals since, caused a certain amount of discomfort. She does not think that the hand is more wasted now than it was eighteen months ago, but she has more difficulty in straightening the ring and little fingers on that side. This, no doubt, is due to the fact that a certain amount of post-paralytic contracture has occurred in the hand similar to that which has been described in ulnar neuritis by J. De Léon (1), who compares it to the facial contracture so common in Bell's palsy, and names the condition "main en pince."

On examination there was found, in addition to the contracture just described, marked wasting and loss of power in the abductor opponens and adductores pollicis, considerable atrophy and weakness of the interossei, lumbricales and hypothenar muscles, with the exception of the abductor minimi digiti. In the forearm the deep and superficial flexors of the fingers were atrophied and weak, whilst the pronator radii teres and wrist flexors had escaped. The pronator quadratus was probably also affected, although of this it was difficult to be sure.

The wasted muscles showed a corresponding loss of electrical excitability. The right deltoid was slightly less powerful than the left, but it was impossible to detect any difference between the strength of the external rotators of the arm on the two sides. There was no evidence of injury to the oculo-pupillary fibres which leave the cord with the first dorsal root.

Over a part of the first dorsal root area on the ulnar side of the forearm there was slight impairment of tactile sensibility, with marked but not complete thermanæsthesia and analgesia. Over a part of the fifth cervical area (see fig. 6) there was slight decrease of sensibility to pain and heat, whilst that to touch and cold was practically normal. Both areas were tested carefully for heat and cold by means of a cautery (in close proximity to the skin) and by an ether spray, with the object of eliminating, as far as possible, the tactile element during the test. In this way it was ascertained that the loss of sensibility to heat over the first dorsal area was more complete than that to cold, whilst the condition over the fifth cervical area was as noted above. The presence of a red-hot cautery close to the skin gave rise to no sensation, either tactile, painful or thermal.

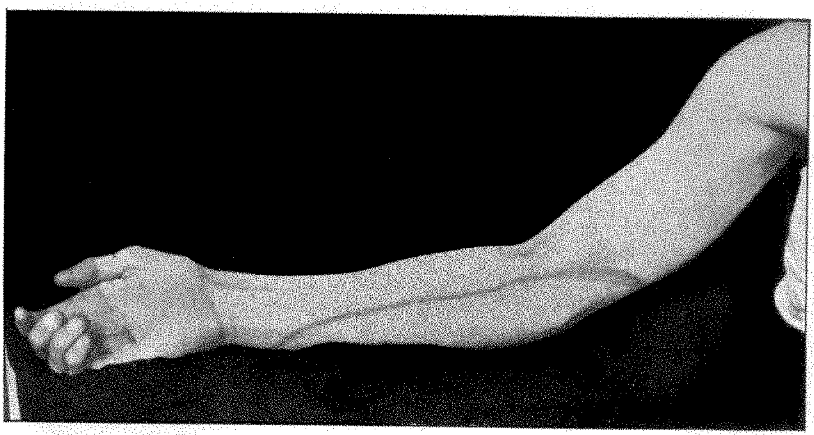

FIG. 5.

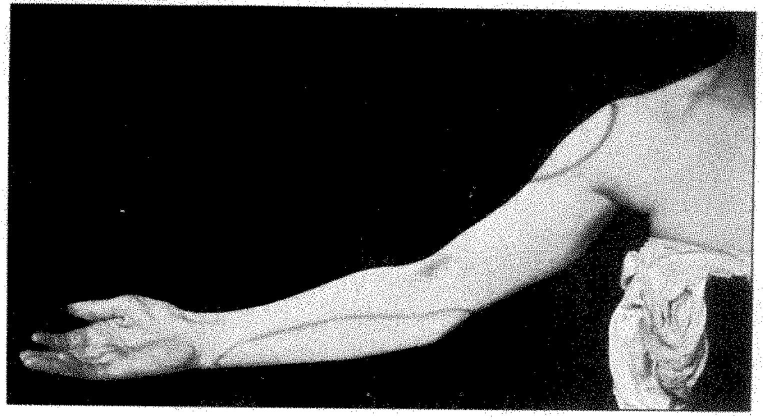

FIG. 6.

On the other hand it appeared that when the wire of a galvano-cautery was held in contact with the skin, and then heated by the passage of a current to a temperature sufficient to raise a small blister but not sufficient to change the colour of the metal, a painful "prick" was experienced by the patient. She did not associate the sensation with heat. This last test, however, was applied after some improvement had taken place in the sensory disturbance. The knee-jerks were brisk, there was no ankle clonus, and the plantar reflexes were flexor in type. The left arm was unaffected, although for a short time she complained of pain in that part. No signs of organic heart disease could be detected.

Under electrical treatment the contracture has much improved, and there appears to be more power in some of the affected hand muscles, while, as above stated, the hyperæsthesia has also undergone some change for the better.

One of the most noteworthy features of the cases just recorded lies in the fact that three of them suggest a lesion of the first dorsal nerve, two of them a lesion of the fifth cervical nerve, and the sixth a lesion of both these nerves. This may be a coincidence, or it may point to a special susceptibility on the part of the lowest and highest roots of the brachial plexus; on the other hand, it is well to remember that a corresponding lesion of any one of the intervening roots does not admit of such ready diagnosis. The anterior primary divisions of the lower four cervical and first dorsal spinal nerves form a small system devoted to the motor and sensory supply of the forelimb, and the overlapping in their peripheral distribution is necessarily greater in the middle than at either end of the system. Thus there is little mingling of the territories of the fourth and fifth cervical or of the first and second dorsal nerves. A striking analogy is afforded by the special nomenclature attached to injuries of the upper and lower trunks of the same plexus, and it is permissible to regard my cases as representing either half an Erb's palsy or half a Klumpke's palsy, the former involving the fifth and sixth cervical nerves, the latter the eighth cervical and first dorsal.

MOTOR PHENOMENA.

A careful study of the sensory and motor phenomena in Case 1 leaves no room to doubt that the incidence of the morbid process was on that part of the fifth cervical nerve which lies beween the junction of its anterior and posterior roots and its union with the sixth nerve to form the upper trunk of the plexus.

In this patient there was no evidence of paresis in the rhomboids, levator anguli scapulæ or serratus magnus, and it is fair to assume that the disease was situated peripheral to the branches which, in part, supply these muscles, and which arise from the nerve as it lies between the scaleni. In Case 3, however, the occurrence of herpes points to an extensive lesion, involving not only the posterior root ganglion, but the anterior root-fibres at their union with the posterior, and if the rhomboids were not affected the explanation must be supplied by a statement of Grenet, who says:—"Assez fréquemment le nerf de l'angulaire et du rhomboide nait du plexus cervical et non du plexus brachial. L'angulaire et le rhomboide peuvent donc rester indemnés dans le cas de paralysie radiculaire intrarachidienne" (2).

The distribution of atrophic palsy in Case 1 supplies valuable evidence of the motor innervation from the fifth cervical nerve, and it is interesting to note that the limitation of this innervation to the spinati and teres minor, a great part of the deltoid, and probably a few fibres of the biceps, is supported by the anatomical researches of Herringham (3). The latter, as a result of careful dissections of the brachial plexus and its roots in a large number of subjects, makes the following statements: (1) It is usually at the junction of the fifth and sixth nerves that the suprascapular nerve is given off, but it is not uncommon to find it springing from the fifth before the junction is made. (2) The sixth, therefore, exercises sometimes an extremely small influence, and sometimes none at all, over the spinati. (3) It appears that the pectoralis major does not usually receive from the fifth. (4) The biceps is supplied by fifth and sixth seven times out of eight. (5) Thirty-one dissections showed no exceptions to the rule that the fifth does not enter into the outer head of the median nerve. (6) The circumflex comes from the fifth and sixth; in six cases from fifth alone; sixth branch often very small. (7) The teres minor is always supplied by the fifth alone. (8) The supinator longus and brevis are usually supplied by the sixth; the fifth is not always excluded.

The upper part of the subscapular muscle also receives a supply from the fifth cervical nerve, but its affection would not lead to a demonstrable disturbance of function.

In Cases 2, 4, 5 and 6 there was present a partial atrophic palsy of certain muscles of the hand and forearm, and although the amount of atrophy varied slightly in individual instances, the same muscles were affected in all. These were the long flexors of the fingers slightly, the interossei considerably, and the muscles of the thenar and hypothenar eminences in varying degrees.

Herringham maintains that the first dorsal nerve sometimes supplies in part the flexores profundus and sublimis, the interossei, the hypothenar and deep thenar muscles, but he does not consider that the superficial thenar muscles receive any innervation from the same source. At the same time he admits the greater difficulty in tracing the fibres of individual roots as far as their terminations in the peripheral as compared with the proximal portions of the limb.

Sherrington (4) finds, too, that the superficial intrinsic thumb muscles receive, segmentally considered, a less posterior motor innervation than the deep intrinsic thumb muscles in the higher vertebrates, and finds in this fact an exception, which he is at a loss to explain, to the rule that the more superficial muscles are supplied by lower segments than those lying deeper in the same part of the limb.

If any value can be attached to clinical cases such as those which form the basis of this paper, the same difficulty does not appear to obtain in man, because in some of them the abductor pollicis showed a very considerable degree of atrophy, equal to that presented by some of the deeper thenar muscles. On the other hand, it was noticeable that a part of the flexor brevis pollicis sometimes escaped.

In Charcot's (5) patient, who suffered from a traumatic lesion of the first dorsal nerve, there was marked atrophy of the hypothenar eminence, less marked atrophy of the thenar eminence, atrophy of the interossei and slight atrophy of the flexors in the forearm, but the author does not state whether the superficial or deep intrinsic muscles of the thumb had suffered more severely. His case, however, supports mine in the distribution of the motor affection.

A comparison of Cases 1 and 3 with 2, 4, 5 and 6 brings out the fact that the wasted muscles in the former were fewer, and generally more profoundly atrophied, whilst in the latter they were more numerous, and sometimes less completely affected. This observation conforms with Sherrington's (6) statement that there is greater overlapping and commingling of the root districts in the muscles of the hand than in those of the shoulder, in the peripheral than in the proximal parts of the limb.

At the same time it must be admitted that the degree of atrophy which obtained in certain of the hand muscles was much greater than might have been at first sight expected if the innervation of only one out of two or more spinal roots had been cut off; but the effect of such a condition on the nutrition of a muscle, especially if untreated over a long period of time, is at present a matter requiring further investigation. The absence of oculo-pupillary symptoms, and of any history of herpes in the instances of first dorsal nerve lesion, justifies the conclusion that the point of injury was situated in the nerve between the junction of its roots and its union with the eighth cervical to form the lower trunk of the brachial plexus. Disease of the spinal cord itself is further excluded by the absence of any signs of spasticity in the lower limbs.

SENSORY PHENOMENA.

There are a few points of considerable interest in connection with the sensory phenomena present in these patients.

The dissociative character of the anæsthesia in the cutaneous root areas was as marked as is often the case in syringomyelia, and may be regarded as evidence of the greater overlapping of the tactile as compared with the algesic and thermal fields in the peripheral distribution of a single afferent root. This fact was pointed out by Charcot some years ago in the case cited above, and was especially referred to by him in drawing a comparison between his patient and examples of syringomyelia.

The algesic area may therefore be regarded, not as the whole territory of root distribution, but rather as that of residuary analgesia after all compensation by overlapping has taken place. For this reason the area alluded to is of smaller dimensions than that over which herpes appears in disease of the corresponding posterior root ganglion, smaller, too, than the region to which pain is referred under similar circumstances; and lastly, smaller than the district in which tactile sensibility is probably but almost inappreciably modified. An interesting observation on the part of Rendu (7) is worthy of quotation in the present context. In a case which was recorded by him as one of reflex neuritis, but the symptoms of which pointed, in my opinion, to a local lesion at the junction of the fifth and sixth cervical nerves, the pain was described as being of two kinds: (1) contusive in character and confined to the shoulder region, (2) intermittent sharp stabs darting from the cervical region to the tips of the fingers. The anæsthesia was limited to the area which was the seat of pain of the first kind.

Turning to the experimental work carried out by Sherrington (8) on "The Spinal Roots and Dissociative Anæsthesia in the Monkey," the conclusions drawn by that distinguished observer may best be referred to in their original words.

(1) "The disturbance of skin sensation produced in macacus by severance of spinal roots is to some extent a dissociative one.

(2) "In macacus the destruction of a single sensory spinal root, at least in the case of certain spinal nerves, entails in a limited skin-area, much smaller than the total skin-field of the root, an abolition of heat sensitivity without abolition, but with some concomitant impairment, of tactual sensitivity.

(3) "In the skin of macacus the 'pain'-field and the 'heat'-field of a single sensory spinal root, at least in the case of certain spinal nerves, are each less extensive than is the 'touch'-field of the same root.

(4) "With the 'heat'-fields and 'pain'-fields of the roots the extent of overlap is greater in some skin regions than in others, *e.g.*, in the hand and foot than in parts of the forearm, thigh and trunk."

The area of dissociative anæsthesia produced by dividing the first dorsal posterior root in macacus is, according to Sherrington's photographs, of smaller extent than that in man, the upper limit falling short of the elbow.

A remarkable feature of my cases was the absence of any subjective sensation of numbness in the hypæsthetic skin. Not one of the patients was aware of his sensory loss until the fact was demonstrated to him. This forms a striking contrast to the subjective numbness in injuries to peripheral nerves, and I would suggest that it may probably be reckoned as an important factor in the diagnosis between a root and a peripheral nerve lesion.

ETIOLOGY AND PATHOLOGY.

It is customary to group under the name "neuritis" all gross lesions of nerves which are not caused by trauma or by the pressure or encroachment of some external morbid process, and this custom finds a close analogy in the application of the term "myelitis" to all transverse lesions of the spinal cord, whether they are of inflammatory or vascular origin. For some reason not easy to explain, similar processes in the brain are better distinguished; cerebral hæmorrhage and thrombosis on the one hand, and encephalitis on the other, are accepted terms amongst diseases of the highest part of the nervous system. Whilst it is clear that there is need for reform in regard to this loose classification of diseases of the spinal cord, it may be urged that our knowledge of peripheral nervous lesions is not sufficiently advanced to warrant any attempt to adopt a more exact terminology than that which is obtained by the title "neuritis." The absence of anatomical evidence to support clinical theory is certainly a serious hindrance to any such attempt, but it is difficult to feel satisfied with a nomenclature which does not draw distinctions between a symptom-complex, suggesting a sudden localised interruption of functional continuity in a single spinal nerve, and a gradual affection of many nerves, probably due to the presence of some morbid influence in the general circulation.

When the help of the microscope is wanting it is necessary to consider the etiology of any particular disease in order to obtain guidance on the problem of its pathology. In Case 1 of my series, short rations and hard physical work are the only items of importance in the remote or immediate previous history of the patient.

In Case 2 the onset of symptoms occurred during convalescence from Malta fever, a disease which bears many clinical resemblances to rheumatic fever, and which is frequently associated with marked anæmia and joint troubles.

Case 3 was the subject of mitral stenosis in the sequel of acute rheumatism.

In Case 4 scarlet fever, followed by two attacks of chorea, were prominent features in the few years immediately preceding the onset of the nervous phenomena.

Cases 5 and 6 were the victims of very severe chlorosis, accompanied, in the latter, by all the symptoms of gastric ulceration.

I submit that the above facts suggest, with reasonable probability, a special liability on the part of these patients to lesions of vascular origin. Such lesions may and do occur in various parts of the body without giving rise to noteworthy symptoms when their incidence is upon vessels of small calibre. Their occurrence, however, in any part of the nervous system cannot fail to produce striking disturbances of function, even when the vessel affected is little more than capillary in size. Embolism of the retinal artery has more than once been recorded in association with chorea (9), and Mr. Marcus Gunn (10) has noted symptoms pointing to hæmorrhage into the sheath of the optic nerve in women suffering from amenorrhœa.

Is it unreasonable to infer that spinal nerves may also be the seat of localised vascular changes, sometimes sudden and sometimes insidious in their onset, and leading to a train of symptoms to which the term "neuritis" is indiscriminately applied? If this possibility is admitted, there is plenty of evidence to suggest that such vascular lesions may occur not only in the brain, spinal cord, and cranial and spinal nerves, but also more peripherally still in the cords of the brachial plexus and the nerves of the extremities. Remak (11), indeed, has proposed the name "acute multiple localised neuritis" for cases presenting the clinical features suggested by that designation, and cites a case where the symptoms pointed to sudden and almost simultaneous lesions of the suprascapular and circumflex nerves on the right side, and of the musculo-cutaneous nerve on the left.

Other cases of musculo-cutaneous palsy, occurring suddenly and alone, are recorded, and in some, such as that described by Hoffmann (12), the area of sensory loss was the seat of subjective numbness. But other nerves are equally commonly affected in this manner, and these are only mentioned in order to emphasise the similarity of the sudden onset with pain, paralysis and atrophy, whether the lesion be situated proximal to, peripheral to, or in the midst of, the brachial plexus.

Many cases of herpes zoster have a striking general resemblance to this group, and are in rare instances (*e.g.*, Case 3) associated with motor disturbances. Although the existence of a specific affection of the posterior root ganglia has been established beyond all doubt by the admirable work of Head and Campbell (13), it is questionable whether some cases of zoster are not dependent on purely vascular lesions, and, indeed, whether some cases cited by those authors in their series of autopsies were not of this nature rather than toxic in origin. They admit the probable vascular origin of at least one case, where an extreme necrotic lesion was found in the 12th dorsal ganglion, but in a case of multiple focal lesions of the cord due to endarteritis obliterans the changes in the diseased ganglion are ascribed to a specific unknown agent, to the influence of which the spinal disease is supposed to have rendered the patient especially predisposed.

I proffer the suggestion that under certain circumstances a vascular lesion may originate (*a*) in a spinal root ganglion, giving rise to herpes zoster and, if the lesion is extensive, to motor as well as sensory phenomena; (*b*) in a spinal nerve, when it will occasion the symptom-complex presented by my cases; (*c*) in a nerve-trunk formed by the union of two or more spinal nerves, resulting in a condition of which Erb's palsy is the commonest example; and (*d*). in a peripheral nerve, causing a localised peripheral neuritis.

Such a view does not preclude the probability that the vascular lesion may be primarily due to some diseased state of the blood or of the blood-vessels, and that its incidence on particular nerves or portions of nerves may be favoured by anatomical peculiarities of which we are at present unaware.

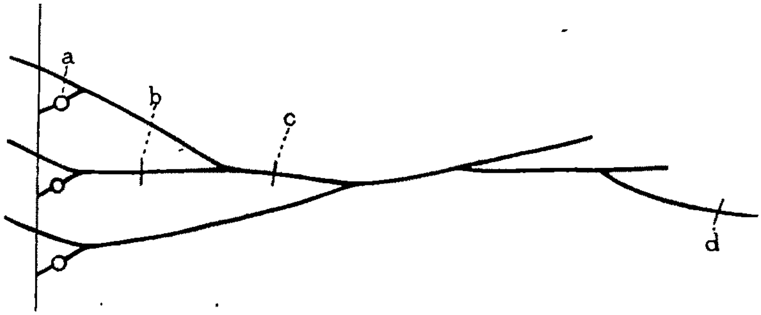

FIG. 7—Diagrammatic representation of the four sites of neuritic localised lesions (see text).

Whatever be the nature of the morbid process concerned in cases of acute or subacute "localised neuritis," it is certain that an extension of our knowledge can only be gained by the careful examination of nerves from their origin to their peripheral distribution when the opportunity is afforded. The practice of only investigating a short length of nerve is not calculated to throw light on the matter, and may be considered analogous to removing a short piece of the spinal cord at an indifferent level for the purpose of studying the nature of a transverse myelitis.

LITERATURE.

Lesions of the brachial plexus, medical, surgical and obstetrical, figure very frequently in English and Continental medical literature, and much has been written about their causation and symptomatology, especially by Erb (14), Duchenne, Klumpke (15), Secretan (16), Dejerine (17), Raymond, Rendu, Bernhardt, Duval (18), Guillain, Grenet, Zuelzer (19,) Stadelmann (20), and others.

These authors refer almost entirely to injuries of its upper and lower trunks, or to injuries affecting all the roots which go to form the plexus. Even the exhaustive monographs on this large subject make but brief mention of uniradicular paralyses. Thus, Duval and Guillain (18) say that uniradicular palsies are very rare, and only mention the "bullet wound" case of Charcot.

Under the heading "Paralysies Uniradiculaires," Grenet (2) says, "Il n'y a pas lieu d'insister sur ces faits qui ne paraissent pas très frèquents."

Secretan's (16) solitary contribution to the subject is contained in the following words:—"Dans un cas de Traube, un osteóme vertebral determine une lésion de la 8e. c. et une atrophie des muscles de la main et de l'avant-bras."

Head (2) says that he has seen a case of herpes zoster in which the eruption over the first dorsal area was associated with palsy of the movements of the hand and fingers, but he supplies no further details.

Cases of zoster in the region of the trigeminal nerve, accompanied by oculo-motor or facial paralysis, of which there are many instances, can hardly be considered comparable, but it is possible that some examples of brachial palsy and herpes collected by Ebstein (22), although imperfectly recorded, may have been allied to one described in this paper.

Lewis Jones (23) has published some cases of atrophic paralysis in one or both hands, and it may be that his Case 6 belongs to the same class as mine, but there is no mention of sensory disturbance.

The sudden and spontaneous onset of Erb's palsy, with no preceding trauma, is not uncommon, and the character of the initial symptoms suggests a similar pathological factor to that of my first three cases, although its anatomical site is not quite identical. At the same time it must be remembered that the difference of a fraction of an inch in the position of the actual morbid process would suffice to provoke a fifth cervical nerve palsy instead of an Erb's palsy. Such variations in position readily account for the minor differences in the physical signs, and often point to a greater or less involvement of the sixth cervical nerve at its junction with the fifth.

The scope of this paper, however, does not admit of reference to the numerous cases of brachial plexus palsy, arising from disease of more than one of its roots, or of the trunks formed by their union.

In conclusion, attention may be drawn to the remarkable fact that whilst Charcot's case is often referred to as an instance of injury to a single spinal nerve, little or no notice has been taken of his interesting observations on the character of the sensory loss produced, observations which have received experimental confirmation by Sherrington, and clinical support, I venture to believe, from this paper.

CONCLUSIONS.—(1) There exists a clinical group of cases in which the symptoms strongly suggest a more or less complete destruction of functional continuity in one of the spinal nerves forming the brachial plexus.

(2) The objective disturbances of sensibility resulting from this lesion closely conform with those observed by Sherrington after cutting a posterior root in a monkey. They differ in some respects from the anæsthesia produced by the division of a peripheral nerve.

(3) The anæsthesia is largely dissociative in character, and does not occupy the whole cutaneous area to which the afferent fibres of the spinal nerve are distributed.

(4) The objective hypæsthesia is not associated with any subjective sensation of numbness, and is consequently overlooked by the patient.

(5) The atrophy of the affected muscles is in excess of what might be expected in view of the fact that many of the muscles receive fibres from two or more spinal nerves.

(6) The condition generally occurs in persons who have at some time been the subjects of a disease affecting the cardio-vascular system. The morbid process is probably vascular in character, and may be sudden or gradual in its onset.

Since writing the above, another interesting case of the kind has come to my notice.

Case 7.—C. H., aged 28, metal turner, complains of loss of power and wasting in his right hand, and of attacks of dull aching pain down the right arm.

Previous history.—Typhoid fever twelve years ago. Injury to skin of right upper arm six and a half years ago, healed in eight days. Six years ago influenza, followed by congestion of the lungs; three months ill. No venereal disease.

Present illness.—About five years ago he noticed gradual wasting of right thenar eminence, preceded by pain in the shoulder and arm. The atrophy and weakness has spread to its present extent slowly.

Now, the abductor and opponens pollicis are much atrophied, the flexor brevis and adductores less so, and there is some wasting and weakness of the interossei, hypothenar muscles and long flexors of fingers. Electrical reactions are altered in corresponding degree. On the inner side of the right forearm there is an area of very marked analgesia and loss of sensibility to heat, with considerable impairment of sensibility to touch and cold. From the upper limit of this area a narrow strip of skin, extending into the axilla, also presents a similar sensory loss (see fig. 8). In this case it seems probable that the lesion is situated in the first dorsal nerve, and involves not only the fibres of that nerve, but also some sensory fibres which properly belong to the second dorsal nerve, and which reach it by a branch from the first to the second. Such a branch is present in a certain percentage of human subjects, and is almost constant in some of the higher vertebrates, but whether its fibres are afferent or efferent I am not aware. The explanation of the condition must be sought in such a supposition, or in two lesions, one involving the first and the other the second dorsal nerve. It is extremely interesting to note that the tactile hypæsthesia in this patient is more marked than in any of those previously recorded, and that he alone of all my cases was aware of his sensory loss. This might have been expected from what has been said above, as the sensory fibres of two adjoining spinal nerves are evidently affected.

The pupils and palpebral fissures are equal. The heart and other viscera are healthy, and there are no nervous phenomena elsewhere.

Note.—The present paper is devoted to the consideration of this disease when its incidence is upon the roots of the brachial plexus; is it possible that the lumbo-sacral plexus may at times be similarly affected, and that some cases of sciatica with muscular atrophy (24) may have an analogous pathological basis?

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DESCRIPTION OF FIGURES.

Figs. 1 and 2.—*Case* 1, T. T. P. Showing area of dissociated sensory loss and atrophy of muscles.

Figs. 3 and 4.—*Case* 2, A. O. Showing area of dissociated sensory loss and muscular atrophy.

Fig. 5.—*Case* 4, E. C. Showing area of dissociated sensory loss and muscular atrophy.

Fig. 6.—*Case* 6, K. P. Showing areas of dissociated sensory loss and muscular atrophy.

Fig. 8.—*Case* 7. Showing the first and second dorsal areas where sensory loss was present.

A CASE OF SCLEROTIC ATROPHY OF CEREBRUM AND CEREBELLUM, OF FAMILIAL TYPE, OCCURRING IN A BOY.

BY J. MICHELL CLARKE, M.A., M.D.CANTAB., F.R.C.P.

Professor of Pathology, University College, Bristol; Physician to Bristol General Hospital.

ARTHUR B., aged 7½ years, was admitted into the Bristol General Hospital on June 29, 1900. The grandmother (mother's mother) was blind until 11 years of age, and then recovered.

The mother said that she had two brothers, both younger than herself; the elder was quite well up to 10 years of age, when he became paralysed, went blind, and died of "lockjaw," aged 12. The second was also well until about 10, when he gradually became paralysed and blind, and died at 13. No more details could be obtained of these patients, and the mother, on enquiry, could learn of no other similar cases amongst her relations. She was an intelligent woman, and was positive that the illness in her brothers' cases presented the same features as in her son. The patient had three brothers, all of them alive and well. The mother had had no miscarriages, and there was no history of syphilis in either parent. The father seemed a steady man, but neither he nor the mother appeared strong, and were rather excitable and of neurotic type.

The boy was quite strong and healthy until 7 years of age, and had never had any bad illness. The first symptoms noticed were that he did not care to go out, and he had slight choreiform jerkings of the arms and legs. The schoolmistress noticed that his hand jumped in writing. His sight gradually failed, and is now very defective, the right eye being especially defective. Eight weeks ago he began to vomit in the morning, but this has now stopped. The face had been drawn to one side. He said queer things, has been very irritable, easily losing his temper with his mother, and his speech has become indistinct lately. The headache has been on the top of the head. He has had no fits, no affection of bladder or rectum; he has been decidedly weak on his legs, easily falls down, and at times will walk right into a wall without observing it. No discharge from ears. He was admitted into the Bristol Hospital on June 29, 1900. He seemed an intelligent boy, and answered questions sensibly. His speech was slow, with intervals between the words, which were also muffled and indistinct. He could sit up in bed, and could walk, but not well. The movements of the legs were uncertain or somewhat ataxic, especially of the right leg, so that he was unsteady, and he also tended to turn and to walk to the left. When walking there were jerkings of the arms, especially of the right arm, and when at rest jerkings, choreiform in character, of both arms and legs occurred. Even at this period, when standing he tended to fall backwards. He could not see to read, but had been able to read before the illness.

The boy was rather thin and badly nourished. His face had an old look. The thoracic and abdominal organs, and condition of the urine, were all normal.

There was no facial paralysis, no oculomotor paralysis, no nystagmus. The pupils were equal, normal in size, and acted well to light and accommodation. Sight extremely defective; he could just count fingers; no change present in optic disc, yellow spot region, or rest of fundus. (This was confirmed by Mr. Walker, Ophthalmic Surgeon to the Hospital.) Hearing normal. No actual paralysis anywhere at this date, but right leg weaker than left, and slight rigidity in each. No muscular wasting. No affection of sensation anywhere to touch or pain. Swallowing normal. Micturition and defæcation normal. No incontinence. Knee-jerks much exaggerated; plantar reflexes active; Babinski's sign present. No ankle clonus.

There was no pain or tenderness over the head or spinal column, and no deformity of them, nor of any other part. No club foot. He left the hospital after two days, as he cried perpetually to go home again and refused his food. During the time he stayed in he appeared to have a good deal of pain in the head. Subsequently he attended as an out-patient.

On August 9 he was decidedly worse; his sight was worse, and he was losing flesh. His mental condition was far worse; he had difficulty in understanding what was said to him, while before he would have understood at once; his memory was bad, and he was much more childish; he would ask his mother for things that he was holding in his hands, and a few minutes after she had given them to him he would forget that he had had them. At times he was very excited. His speech was more indistinct.

He was now apparently a little deaf, but it was difficult to be sure of this on account of the mental dulness. He kept his mouth open, and his lower lip dropped. Otherwise there was no facial or oculomotor palsy; no nystagmus; pupils normal. There were still slight irregular jerkings of limbs, but not so marked. He walked with an uncertain, ataxic gait, weak and unsteady, and had a tendency to fall backwards. He was never still, but kept walking backwards and forwards. Both legs were rigid, with exaggerated knee-jerks, and with extension of toes in plantar reflexes, but no ankle-clonus. The great toes were in constant position of hyper-extension. There was now a tendency for him to wet his bed.

In September there was incontinence of urine; he passed his fæces into his clothes, and was unable to feed himself.

On October 25.—Condition worse. His sight had been steadily failing, and he was now quite blind, and remained so. At the same time the optic discs and fundus oculi remained normal, and the pupils reacted to light (feebly). The pupils were now large, and slightly unequal. Mentally he was more dull, but happy, laughing and chuckling to himself; he recognised a penny, knew my name, and put out his tongue when commanded, but this was about the extent of his powers. His mouth was open, saliva dribbling from it. He could just stand alone, balancing himself with his feet wide apart, and falling backwards at the least touch; he could only walk with support, taking short steps with his feet wide apart. He could not sit up alone, falling backwards. The knee-jerks were greatly exaggerated, there was slight ankle clonus, and marked rigidity of both legs.

In November he had an attack of herpes zoster, affecting the fourth and fifth left intercostal spaces; this was accompanied and followed by much pain. He was quite blind, and at times cried out with pains in the head; there was no vomiting. He could swallow fairly well; his speech had become very indistinct, and except when he cried out for food or because of pain, he spoke very little. The cranial nerves were unaffected. He was unable to feed himself. He had somewhat more control over the sphincters than in the previous month. He could just stand, but tended to fall backwards, and when he tried to walk he went backwards until he fell. The arms were now rigid, with exaggerated deep reflexes; spastic rigidity in the legs was very marked, with ankle and knee clonus on each side.

In December he had lost the power of standing or walking unsupported; when placed upon his feet he fell backwards at once.

His speech was very slurred and indistinct, saliva constantly dribbled from his mouth, and during sleep he made munching movements. Both arms and legs were the seat of marked spastic contracture, and were affected, the legs especially, with painful cramps.

In January he had an access of severe pains in the head and of painful cramps in the legs, and apparently in the abdominal muscles. He also suffered from obstinate constipation. He could not sleep, and cried out day and night, so that he was admitted again into the hospital. He was now quite bed-ridden, helpless, and it was impossible to make him understand anything. Both arms and legs were rigidly contracted, the latter being flexed at the hips and knees and drawn up upon the abdomen. There was no affection of sensation. The pupils were moderately dilated; there was no change in the optic discs. He was much wasted, had incontinence of urine; there were no bed-sores. He cried out constantly for his mother, and would take food from no one else, so that she took him out of the hospital the next day. He died shortly afterwards, constantly crying out or screaming some days before death.

Permission was given after some difficulty to examine the head only, and this examination was made in a slum under very adverse conditions, and I could only take away with me small portions of the brain, and not the whole of it, as I should have wished.

I could not get leave to examine the cord. This must be my excuse for the imperfections of the pathological report.

On examination the brain was small, the dura mater healthy, the pia-arachnoid was not decidedly thickened, but its vessels were in places injected, especially over the posterior part of the brain. There was no evidence of past or present meningitis. The cerebro-spinal fluid was present in excess. The cerebral cortex was somewhat injected. The brain was normally developed, and there was no obvious change in the arrangement of the convolutions, but those of the occipital lobes and motor area were small. As a whole the posterior pole of the hemispheres was unduly small. The optic nerves and tracts, the cranial nerves generally, and corpora quadrigemina appeared healthy.

On cutting into the cerebral hemispheres, the chief naked-eye changes were a patch of *recent* softening in the left internal capsule, involving the greater part of it, and a tough, indurated or sclerotic condition of the white matter of the occipital lobes, which was grey, dense, hard and firm. The occipital cortex was paler and thinner than normal, and this was true in less degree of the motor cortex. The white matter of the ascending frontal and parietal convolutions was firmer, and the right internal capsule greyer in colour than normal. The basal ganglia and subthalamic regions appeared healthy. The ventricles were somewhat dilated, their ependyma healthy.

The cerebellum was rather small; externally it had a healthy appearance; the cortex looked normal on section, but the white matter showed an even greater sclerotic change than that of the occipital lobe, being dense, hard, tough, grey in colour, and cutting like tough fibrous tissue, almost creaking under the knife.

No new growth was anywhere found, nor any sign of a gummatous formation. The bones of the skull were normal, and the calvarium not unduly thickened. The vessels at the base were healthy, and contained no clot. They had the normal arrangement.

The bones at the base and the tympani were normal. Portions from the cerebellum, both occipital lobes—outer surface and in region of calcarine fissure—motor convolutions, and præfrontal areas on each side, optic nerves, region of internal capsules, crura cerebri, pons, medulla, and upper end of cervical cord, were examined microscopically.

Nissl's stain, Pal-Weigert, with carmine, Marchi's method, Van Gieson's stain, logwood and eosin, were used for cortex cerebri and cerebellum; and for pons and medulla, Pal-Weigert and carmine, and Marchi's method.

In the cerebrum, the most pronounced changes were found in the occipital cortex, and these were by far most intense in the neighbourhood of the calcarine fissures. The pia-arachnoid, under the microscope, appeared slightly injected, and the larger vessels distended. The superficial layer of cortex, and the first and second layers of granule cells, appeared healthy. The whole cortex was narrowed, and the pyramidal cells were in all stages of degeneration and atrophy. The large pyramids and deepest layer of cortex were most affected; next the small pyramids.

The changes were not uniform, but patchy in distribution.. There were numerous small spaces in the grey matter (where atrophied cells had disappeared ?). The vessels showed a moderate degree of injection, the neuroglial cells were increased in number, and in the parts in which the destructive process was most advanced there was a round-celled infiltration from the vessels, and phagocytes could be seen attached to the pyramidal cells in some instances. Vascular changes were more marked in the layer of white matter immediately subjacent to the grey; here many vessels were crowded with leucocytes, which were passing in numbers into the perivascular space and surrounding tissues. In the white matter, in very few places in the grey, there is to be seen extremely abundant proliferation of the endothelial cells lining the perivascular space, so that the latter was crammed with large endothelial plates with distinct small round nuclei. The vessel walls themselves were mostly normal, but some showed slight thickening. There was no sign in any of endarteritis.

In the white matter of this lobe, extensive areas were found in which, with the above vascular changes, the tissue consisted of a dense network of spider cells, with large, richly-branched, and coarse processes, forming an almost myxomatous-like tissue, but obviously composed of the greatly-proliferated neuroglial cells of the part. In these areas the white fibres had practically disappeared, and in others in this lobe, with less advanced change, were few in number. Sections did not stain in Marchi's fluid, but by Pal-Weigert stain the fine tangential fibres of the cortex were greatly reduced in number, in places almost absent, and in the deeper parts of the white matter there were areas in which the medullated fibres passing from convolutions were degenerated.

In sections from the motor convolutions there were similar changes, but less marked; the distribution was more partial and less intense in degree. In the cortex, the large pyramidal cells and the multipolar cells of the lowest layer were chiefly affected, there being a considerable number of cells in different stages of degeneration in these layers; on the other hand, there were numerous healthy cells. To a less extent the layer of small pyramidal cells was also affected. The capillaries were injected in places, with emigration of leucocytes and increase of neuroglial cells (Nissl stain).

The vascular changes in white matter were slight, and there was an absence of proliferation of endothelium of lymph spaces. As in the occipital cortex, the underlying white substance was most affected in those places where the changes in the grey matter were most evident. In the most affected areas the tangential fibres of cortex appeared deficient in number (Pal-Weigert).

Sections from the præ-frontal area showed that the grey and white matter were practically normal, with the exception that there were a few scattered pyramidal cells in which the protoplasm had a swollen, glassy appearance, the Nissl granules were absent, and the nucleus obscured, or excentric in position, and there were also a very few atrophied pyramidal cells. By Marchi's method, sections from cerebrum stained badly, and failed to give any additional information.

Cerebellum (Nissl stain).—Granule layer normal, and at first sight Pinkinje's cells normal, but on examining several sections it became probable that they were really somewhat deficient in number when compared with the normal cerebellum. Although the vast majority of them had a healthy appearance, some were rounded in shape, had lost their processes, stained deeply and uniformly, so that the granules could not be distinguished, and nuclei were obscured.

(Pal-Weigert).—In small folia, fine fibres of white matter stained normally, but in tracing them down they passed in several instances into patches, in which they disappeared (sclerotic areas ?), to emerge again in greatly reduced numbers. The fibres could not in any case (probably from change in direction) be traced a great distance, but in the larger stems, just above the point beyond which they could not be traced, the medullated fibres sometimes became tortuous and separated by wider intervals.

(Marchi).—By this method, sparsely-scattered degenerated fibres were found in all sections; most abundant in small, but traced in some cases into medium-sized or large stems of folia.

In layer of white matter subjacent to grey cortex, could be seen in many places injection of vessels and infiltration with leucocytes, and in the larger stems of the white matter there was, in addition, increase of the interstitial tissue. (Van Gieson and hæmatoxylin and eosin stains.)

These changes affected middle and both lateral lobes. On the whole the pathological changes in the cerebellum were not so marked under the microscope as the very striking naked-eye changes had led one to expect. In the crura, cerebri, pons, medulla, and beginning of cervical cord, sections stained by Pal-Weigert showed a complete and absolute degeneration of the pyramidal tract on each side—no healthy fibres appeared to be left; but by Marchi's method each pyramid was found to contain 20 to 30 fibres which took this stain, and had presumably degenerated more recently.

In the pons (Marchi's stain) there were found a few scattered degenerated fibres in the lateral and especially in the mesial fillet, on each side, and a few also in each superior cerebellar peduncle; but these were only few, the vast majority of fibres being healthy. In sections through the medulla there were also a few scattered degenerated fibres in the restiform body on each side, a very few in the reticular formation, in the issuing left sixth nerve-root, and in the peduncle of the left flocculus cerebelli.

I much regret that the *post-mortem* examination was unavoidably so imperfect, and that I was not able to obtain the cord. From the sections at the decussation of the pyramids, and immediately below it in the cervical cord, it appears plain that the degenerations were entirely descending, and that there were no ascending ones.

To sum up briefly the whole case: Clinically the disease was characterised by appearing without ascertainable cause in a previously healthy boy of 7, two of his mother's brothers having died from a disease having like symptoms and running a similar course, at the ages of 12 and 13 respectively (and his grandmother having been blind in childhood and recovered). The first symptoms were choreiform jerkings of limbs and failure of sight, going on to ataxy of cerebellar type, blindness, without affection of lower visual segment or optic neuritis, indistinct speech, increased tendon-reflexes and spastic rigidity, a kind of forced movements, constant tendency to fall on the back of his head, with gradually increasing mental dulness, ending in paralysis of all limbs, spastic painful contractures, progressive dementia, emaciation, and death from exhaustion.

Pathologically, so far as was ascertained, on both sides of the brain there was destruction, atrophy of cortical neurones in grey matter, and sclerosis of white matter of occipital lobe, most marked on mesial aspect (calcarine fissure); the same changes, but to a less degree, in motor convolutions, yellow softening in left internal capsule, complete degeneration of pyramidal tracts on both sides, sclerosis of white matter of cerebellum (both sides), and a few scattered degenerated fibres in fillets, superior cerebellar peduncle and restiform body.

A few general considerations as to the nature of this case may not be out of place. In many respects it corresponds to some of the cases dealt with by Dr. Collier in his valuable paper on cerebral diplegia,[1] and especially to those examples of cerebral diplegia of post-natal origin with generalised cerebral rigidity, but differs from them by the addition of cerebellar symptoms and peculiar form of blindness. The first point to be settled is the question whether the history is sufficiently definite to warrant the view that the case belongs to a "family" disease. As the other cases were not seen, there is only the mother's statement to go upon, and with regard to that it can only be said that she was an intelligent woman, and that the symptoms were sufficiently distinctive to avoid confusion. One could not, however, say that the blindness was due to exactly the same cause as in the present case, as the other patients may have had cerebral diplegia, with the optic atrophy that not uncommonly accompanies it. Admitting, however, that the three cases occurring in two generations of the family, with, at any rate, a striking correspondence in symptoms and age at onset, justify one in regarding them as belonging to the familial class of nervous disease, then the present case may be assigned to a group of more or less similar diseases of the brain occurring in childhood or adolescence, and presenting considerable diversity in range of clinical symptoms in individual instances. The age at onset is important, as, in order to avoid complication by the inclusion of congenital defects or diseases of the brain, or injuries arising in various ways during parturition, it is better, provisionally, at all events, to exclude cases in which the first symptoms of disease are noted in infancy.

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[1] Brain, vol. xxii., 1899.

By thus narrowing the field of observation, and further restricting it to familial diseases, the affections which stand in nearest relation to the case above reported are (1) certain cases of cerebral diplegia beginning in childhood, and (2) probably some cases of family spastic paraplegia. Taking the latter first, in the series of twenty-nine cases collected by Lorrain [1] the average age of onset was 8 to 15 years. No pathological changes are given, but the author draws the important conclusion from his cases that the family diseases of the nervous system are not sharply defined from each other, but are connected by transitional forms. In two cases reported by Mdlle. Pesker,[2] of two brothers, we find such a transitional form, for, in addition to spastic paraplegia, there was intention-tremor and ataxia in the arms, affection of speech, and decided mental weakness (in Lorrain's cases the mind was unaffected) ; and in the case of one brother, who died, besides changes in the posterior columns and Clarke's columns in the cord, there was deficiency in nerve-fibres and in development of ganglion-cells in the cerebral cortex.

Cerebral diplegia, although rarely, does occur in familial form, and many cases are now recorded.[3] The symptoms in cerebral diplegia, in the particular form now under consideration, may be put very briefly as general muscular rigidity, spastic contractures of limbs, exaggerated deep reflexes, more or less paralysis, tremors, affection of speech, and often choreiform or athetotic movements, optic atrophy, with more or less defect of intelligence. The mental affection varies very greatly, in some cases being slight until towards the end of the illness, in others being marked throughout, like those reported by Homen,[1] where, with similar bodily symptoms to those just detailed, the mental changes were so pronounced as to make the cases resemble juvenile general paralysis. It is true that in these particular cases the cause was probably congenital syphilis. The course of the disease is progressive, the duration varying.

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[1] *Thèse de Paris*, 1898

[2] *Revue Neurologique*, vol. viii., p. 348.

[3] See "Dercum."—*J. of Nerv. and Mental Dis.*, 1897, p. 398-9, where several references are given.

The symptoms in particular cases will vary according to the part of the brain on which the chief stress of the disease falls. In the majority of cases, this will be on the motor convolutions, with more or less accompanying mental changes, according to the degree of affection of the præfrontal area. In Homen's cases just quoted, the chief changes were found in the frontal lobes.

The peculiar point which would seem to make the case I have reported a very exceptional one is that the cerebellum was also affected, and consequently cerebellar symptoms were prominent through a large part of the course of the disease, and in addition, the changes in the cerebrum being most pronounced in the occipital lobe, there was the striking symptom of blindness without any change in the eye itself or in the optic nerve.

I have not been able to find this symptom recorded in any other case in the limited search I have made into the literature, but I have not attempted an exhaustive one. In Dr. Collier's paper,[2] he quotes Richardière as saying that the atrophy in cerebral diplegia has a special preference for the occipital lobe in many cases, and he also says that in connection with atrophy of the hemispheres there may be marked atrophy of the cerebellum.

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[1] *Neurol. Centlbltt.*, 1897, p. 864.

[2] *Loc. cit.*

The cases that approach most nearly to mine in clinical symptoms are the following:—

Drs. Pauly and Bonné[1] have published an account of a family in which three sons suffered from the same nervous affection; two others were stillborn, and five daughters were healthy. The chief symptoms were spastic condition of legs, intention-tremor, speech-disturbances, optic atrophy, nystagmus, spastic, staggering gait, with absence of affection of sensation of the sphincters or of intelligence. Deep reflexes exaggerated to clonus. The disease began in the eldest patient with staggering, in the second with spastic gait, and in the youngest with nystagmus. The authors conclude that their cases do not belong to a family form of insular sclerosis, nor to hereditary cerebellar ataxy, nor to family cerebral sclerosis, and regard the clinical symptom-complex as a transitional one between hereditary cerebellar ataxy and cerebral diplegia.

I have also seen a short abstract of a paper by Cestan and Guillain,[2] in which two cases of family spastic sclerosis are described. The patients were two brothers; one of them had always had an abnormal gait, and at the age of 15 speech disturbances appeared; some months later the gait was strikingly "spastic cerebellar."

With regard to the pathological changes in my case, their nature is not a specific one; in other cases more or less similar changes have been found. Their distribution, however, is unusual in its wide extent, in affection of cerebellum, and absence of implication of frontal lobe. In respect of the cerebellum it is certainly worthy of remark that the microscopic changes in the cerebellar cortex were so insignificant, when one bears in mind the marked cerebellar symptoms, and also the advanced degree of sclerosis of the white matter at the base or stems of the lobes.

The cause of the disease was not congenital syphilis; the history was absolutely decisive on this point. Although the proliferation of endothelium in perivascular spaces is seen in syphilis, it also occurs under other conditions, and the absence of any change in the arteries themselves is very strongly against it, setting aside the absence of any gross syphilitic lesions.

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[1] *Revue de Méd.*, xvii., 3, p. 201, 1897.

[2] *Revue de Méd.*, No. 10, 1900.

In the absence of syphilis, an early form of general paralysis is extremely unlikely, and the distribution of the changes in the brain, and especially the escape of the frontal lobes, is not that of general paralysis, although the vascular and perivascular changes, in combination with the atrophy of the cortex, present a resemblance to it.

The microscopic appearances also differ from those found in most cases of cerebral diplegia[1] in the more pronounced vascular changes and sclerosis of white matter of the affected lobes, the essential change in these cases being the atrophy of the cortical neurons. As in most cases of this kind, it is extremely difficult to decide whether the change is a primary one in the cortical neurons. and the sclerotic and vascular changes merely secondary to the disappearance of the parenchymatous elements, or whether on the other hand the disease is due to a poison circulating in the blood, the alterations in the vascular system being first produced, and the destruction of the cortical neurons secondary to them.

It is well to bear in mind that the sclerotic process with vascular and perivascular changes was more pronounced in the white than in the grey matter in this case. It is, I suppose, conceivable that even when the primary change is in the neurons, the amount of secondary sclerosis and vascular change may vary very much in intensity in different cases, at one end of the scale being very slight, at the other constituting a predominant feature of the pathological alterations.

In favour of the view that the condition here is primary in the neurons, is the character of the onset—insidious, without fever or other constitutional disturbance, not preceded by one of the specific fevers, all points unlike the action of a toxin. The course of the disease, though not long compared with that of some other family diseases, is more consonant with this view, and there is the evidence of other cases in the family. The fact, also, that in this case

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[1] See Collis, *loc. cit.*

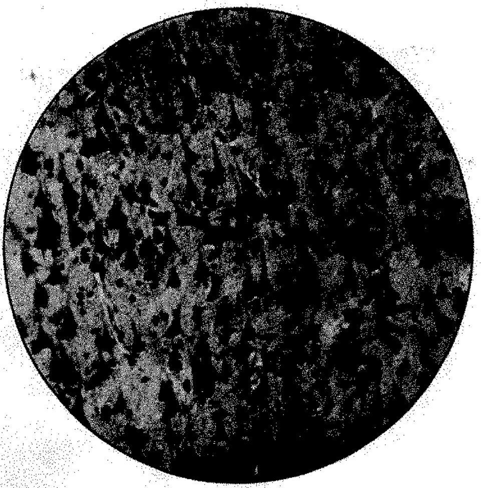

FIG. 1

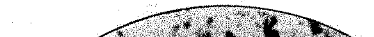

FIG. 2.

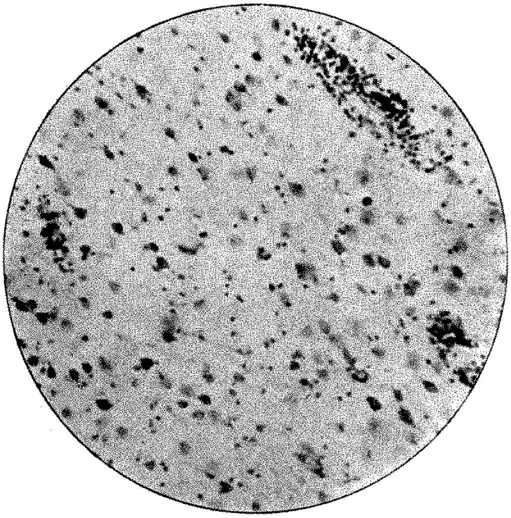

Fig. 3.

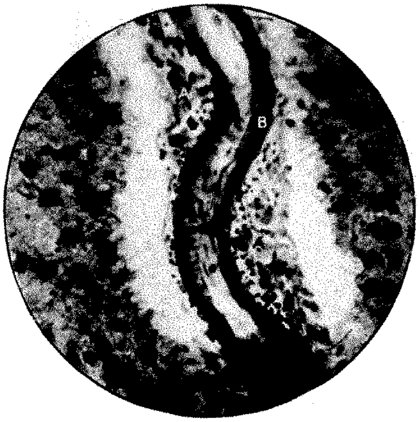

Fig. 4.

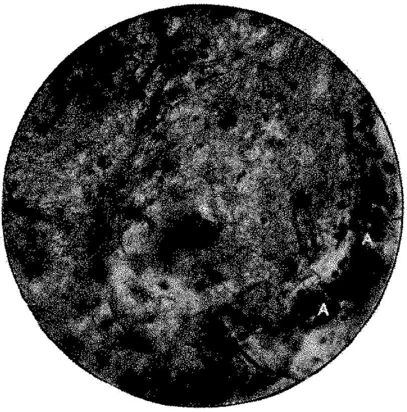

Fig. 5.

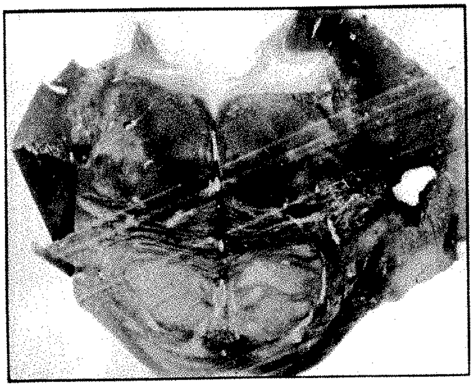

Fig. 6.

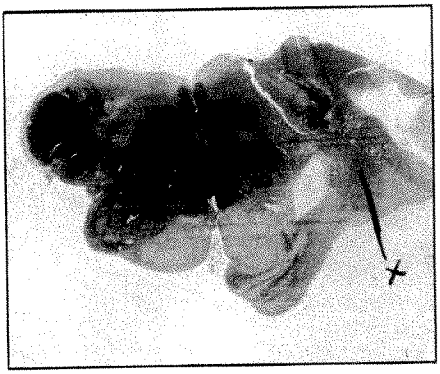

Fig. 7.

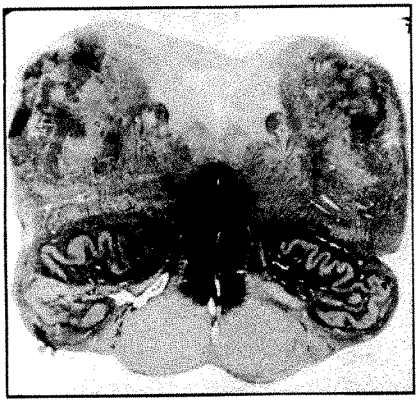

Fig. 8.

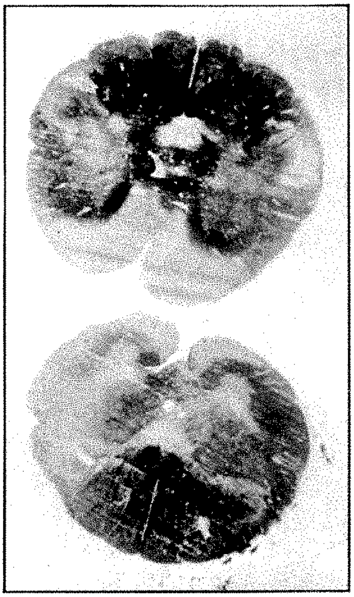

Fig. 9.

the disease appeared at an age some years earlier than in the preceding generation, tells in the same direction. The distribution of the disease in the brain is difficult to explain in any other way, and in connection with this it is to be noted that though vascular changes predominate in the white matter, there is a close correspondence between the affected areas of grey and white substance, those of the latter subjacent to the most altered portions of grey matter showing the most advanced changes.

Perhaps the above case may be best described as clinically intermediate between cerebral diplegia of postnatal origin and hereditary cerebellar ataxy, with the occurrence of the peculiar form of blindness due to the special incidence of the disease upon the occipital lobes. As similar types of disease appear to reproduce themselves with some fidelity, this peculiar combination of clinical symptoms may again be met with.

My best thanks are due to Mr. James Taylor and Mr. Moline for kindly taking the photographs for me.

EXPLANATION OF PHOTO-MICROGRAPHS.

FIG. 1.—Section of cortex of præfrontal area, apparently normal, for comparison with

FIG. 2—Section of occipital cortex, showing advanced degeneration and atrophy of pyramidal cells. A vessel at left-hand margin shows proliferation of endothelial cells of perivascular space, and another further to the right (at lower margin) shows infiltration of round cells. Two or three pyramidal cells can be seen which have retained their normal shape.

FIG. 3.—Section through junction of gray and white matter. The latter (right half of figure) shows round-celled infiltration around vessels in subjacent layer of white matter. Left half of figure shows degenerated cortex.

The above three sections are stained by Nissl's method; the magnification is about 180, in order to get a fair-sized field. Figs. 4 and 5 are stained with logwood and picro-fuchsin.

FIG. 4 shows an artery from sclerosed white matter of occipital lobe. The wall of the artery itself is normal, but on each side of it, in perivascular space, is a mass of cells, chiefly composed of large endothelial cells from lining of space, with some leucocytes amongst them. The dark cells in the part of the field to the left of the artery are spider-cells.

FIG. 5 shows the network of richly-branched cells, which make up the dense sclerotic areas, and to the right, marked AA, is a small vessel almost hidden by the proliferation of the endothelium of perivascular space. This section is under a higher magnification.

FIGS. 6, 7, 8 and 9 are sections from various levels of pons, medulla, and at decussation of pyramids, which are stained by the Pal-Weigert method, and show absolute and complete degeneration of both pyramidal tracts. At x in Fig. 7 is a small tract of degenerated fibres in the peduncle of the flocculus.

THE PATHOLOGY OF SO-CALLED ACUTE MYELITIS.[1]

BY H. DOUGLAS SINGER, M.D., M.R.C.P.

THE subject-matter of this paper has been arranged in the following order:—(1) A brief historical account of the views which have been held with regard to the pathology of so-called acute myelitis; (2) a description of the morbid anatomy of the spinal cord in two cases which died within eight weeks of the onset of the symptoms; (3) some remarks upon the etiological and clinical features of the disease which bear upon the conception of its pathology. My thanks are due to Dr. J. S. Risien Russell for permission to make use of one of the cases, and also to Dr. J. S. Collier, who, besides preparing the sections and photographs of the two cases, has helped me very materially in the preparation of this paper.

HISTORICAL.

Prior to the year 1866 it was universally believed that softening, both in the brain and in the spinal cord, was due to an acute inflammation; the two conditions were described respectively as acute cerebritis and acute myelitis. In that year Dr. Bastian for the first time ascribed "softening of the brain," in Reynolds' "System of Medicine," to what has ever since been regarded as its true cause, *viz.*, occlusion of blood-vessels. No such change, however, was made in the conception of the pathology of acute myelitis, and the view which attributes the condition to an inflammatory process has continued to obtain in the minds of the majority of neurologists up to the present day, in spite of the close resemblance of the disease, both clinically and anatomically, to "softening of the brain." In 1882 Dr. Bastian, writing in the first edition of "Quain's Dictionary of Medicine," for the first time published his opinion that softening of the cord is due in the great majority of cases to thrombosis of spinal vessels, the result of disease of their walls. In this article he divides the cases of so-called acute myelitis into two groups, "softening of the spinal cord (thrombotic)" and "acute myelitis." With regard to the latter Bastian adds: "True inflammatory softenings very rarely occur as pathological states; they are met with rather as secondary changes after one or other of the following primary lesions or morbid conditions . . . . (*a*) around and from wounds or other traumatic lesions of the spinal cord; (*b*) starting from some blood clot or tumour situated in or pressing upon the substance of the cord. . . . . ; (*c*) myelitis peripherica in spinal leptomeningitis; (*d*) pyæmia."

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[1] Read before the Neurological Society, March 18, 1902.

Bastian again published this in 1886 in his book "Paralyses; Cerebral, Bulbar and Spinal," but very little notice appears to have been taken of his views in England, with one exception. R. T. Williamson published a paper, on "The Relation of Diseases of the Spinal Cord to the Distribution and Lesions of the Spinal Blood-vessels" in the *Medical Chronicle* for 1894, wherein he entirely supports the thrombotic view. Apart from this, most of the modern English text-books adopt the older theory of inflammation. Fagge discusses the question at some length, but comes to no definite decision. Gowers maintains the inflammation theory for the majority of cases, but in the last edition of "Diseases of the Nervous System" admits that possibly some are due to thrombosis, as in cases published by Williamson and Schmaus. Frederick Taylor, in "Allbutt's System of Medicine," mentions Bastian's views, but dismisses them in a few words. Among Continental authors, Hochhaus in 1899, Mager in 1900, Schmaus and Sacki in 1901, all adopt the view that the disease is essentially an inflammation of the spinal cord, although all describe the gross vascular changes, generally without leucocytal inflammation, and in spite of the fact that Mager and Schmaus have both published cases showing syphilitic arteritis. The absence of small-celled infiltration is a striking feature in all records, and this has been the case even in a cord examined eight days after the onset of symptoms. On the other hand, Oppenheim, Marie, Bruns, Ziegler and Rosin adopt the view that most cases are due to thrombosis. Many have been published, also, in which this condition was definitely proved.

Of recent years there has been a growing literature, especially in France, in which acute inflammation of the spinal cord is ascribed to the action of bacteria or their toxins. Various organisms, especially streptococci and staphylococci, have been cultivated from the softened cords in man; acute myelitis, generally of a disseminated character, has also been produced in animals by inoculation, both with organisms and with their toxins. While allowing that probably some cases of this nature do occur in man, they must be very rare, and it should be borne in mind that there is often a possibility of infection of the damaged tissue subsequent to the occurrence of the lesion, especially in cases where there is severe cystitis. It is, moreover, inconceivable that staphylococci, for instance, could grow in such conditions without forming an abscess, a result which microscopic examination certainly fails to reveal in the majority of recorded instances of so-called acute myelitis.

Morbid Anatomy of Two Cases.

A. B., a male, aged 56 years, was clinically a typical case of what is generally known as Acute Myelitis, and the history may be briefly summed up as follows:—He contracted syphilis two years before the onset of the illness from which he died. In 1901 he went into a surgical home to have a cyst connected with the right elbow-joint excised, being otherwise in normal health. The operation was successful, and the wound healed by first intention, running an afebrile course. On the fourth day after the operation he felt some numbness and tingling in the lower extremities, and in the course of a few hours developed a complete flaccid paraplegia, complete anæsthesia of the legs, the highest level of any sensory change being the eighth dorsal root area, and retention of urine. In a few days this gave place to a spastic condition of the legs, with complete incontinence of urine and fæces. He later developed bedsores and cystitis, after which he was admitted to the National Hospital, where he died about seven to eight weeks after the onset of the nervous symptoms, without any further development to indicate a spread of the lesion. The autopsy revealed nothing abnormal to the naked eye in the condition of the spinal cord, with the exception that possibly there was more congestion in the veins of the lower dorsal and lumbar regions than usual. After hardening, a gross lesion was found in the cord, which was limited to the eighth, ninth, and tenth dorsal segments. In the eighth segment was a patch of softening situate in one anterior column of the cord, while a little lower was another and smaller patch in the posterior column. There was no other specially softened spot, but the Marchi stain demonstrated that the nerve elements, practically throughout the transverse section of the cord in the eighth and ninth dorsal segments, were degenerated. Above and below these levels were pure ascending and descending degenerations.

The most striking feature in sections stained with hæmatoxylin and eosin was the condition of the blood-vessels. Both internal and external coats showed extreme thickening, amounting in places to complete obliteration of the lumen. The larger vessels showed a small-celled infiltration, limited to the perivascular lymph spaces, and there was multiplication of the nuclei of both internal and external coats. In short, the vessels showed a typical picture of syphilitic arteritis, nor was this change limited to the vessels at the level of the lesion; similar, though as a rule less marked, evidences of arteritis were present in sections both above and below. With regard to the nervous tissues, they presented the usual appearances, which have been so often described, but there are two points upon which I particularly wish to lay stress, viz., there was no small-celled infiltration, and there was no obvious increase of neuroglia tissue nor multiplication of its nuclei. Thus, the appearances were quite distinct from those produced by acute inflammation of any tissue, in which, it will be remembered, stasis occurs in the capillaries and small veins, and the emigration of leucocytes occurs from these vessels; consequently the white cells invade not merely the perivascular lymph spaces, but the pericellular lymph spaces in which the capillaries run.

It may be urged that the examination was made too long after the occurrence of the inflammation for these signs to be present. The result of an acute inflammatory process in such a position must be either suppuration, resolution, or the extremely improbable transformation into a chronic process with multiplication of the connective tissue of the part; none of these has occurred in this case. We have to deal, it is true, with an inflammation, but it is a chronic one, involving, not the spinal cord proper, but the walls of the blood-vessels, with the visible result that in many places their lumen is obliterated. The logical conclusion, therefore, is that the nervous tissue, being deprived of its blood supply, has undergone either necrosis or degeneration, according to the degree of completeness of its starvation.

The second case, C. D., was a male aged 12 years. I unfortunately did not see this case during life, and have only been able to secure the spinal cord, while the clinical history available is very meagre. The patient was, at the time of the onset of the paraplegia, suffering from a condition which proved *post mortem* to be gummatous meningitis, the result of congenital syphilis. I am assured that the paralysis of the legs developed rapidly in the course of two or three days, and that death occurred about seven weeks later. The cord, with the theca, was hardened in formalin, and sent to me ten days later. Nothing abnormal was to be seen with the naked eye, but on examination by the Marchi method a transverse lesion was found in the sixth dorsal segment, extending only a very short distance in a vertical direction. On microscopic examination the lesion presented some similarities to that described above; that is to say, the vessel walls showed practically identical changes, with small-celled infiltration limited to the perivascular sheaths. It differed, however, in that none of the larger vessels were completely occluded, although some of the capillaries appeared to be so; further, in the place of the softened patches described in the previous case, there was overgrowth of the perivascular connective tissue, especially marked in the posterior columns close to the commissure, the posterior median vessels being surrounded by a greatly thickened coat, which rendered the septum as large as the anterior median fissure. This difference is of special interest in that it very possibly corresponds with what is seen in the brain, where, as the result of thrombosis, in adults there is usually softening, in children and infants very often sclerosis. It should also be mentioned that in this case the vessels in other regions of the cord were practically normal. In this specimen, as in the last, there is, then, no evidence, in the way of leucocytal infiltration or multiplication of neuroglia tissue, to indicate any inflammation of the spinal cord itself, whereas the condition of the vessels amply accounts for the degeneration by reason of the deficient blood-supply to the tissues.

ETIOLOGY AND CLINICAL HISTORY.

In reading through the causes of this disease in text-books, one gathers what, I venture to think, is an entirely erroneous impression as to the etiology.

Much stress is laid by all authors upon the influence of exposure to cold, injury, overwork, suppression of menstruation, and specific infectious diseases. With a view to obtaining some data upon this question, I examined the records of cases of acute myelitis at the National Hospital for the past six years, but found that in many cases the notes are not sufficiently definite to permit of their description under this name with perfect certainty. Consequently I have decided to give particulars only of cases which have come under my own observation in the last two years, small though their number be. The total was 19, all of whom were males. In 15 there was a definite history of syphilis, occurring in 12 at intervals of one to three years from the onset; in 3 six and a half, ten, and twelve years respectively before the occurrence of the paraplegia. Of the remaining 4 cases, in 1 syphilis was denied, but could not be excluded whilst no other cause was discoverable; 2 occurred in old people of 59 and 73 years of age, who had marked thickening of the arteries; 1, a lad aged 19, in whom venereal disease could be definitely excluded, had had some indisposition, lasting two or three weeks, before the onset of the nervous symptoms. He had also been vaccinated, and had "taken" well, one week before.

These figures, small though their number, can certainly not be the result of coincidence; they are moreover supported by other observers, notably Erb and Rosin, with regard to the frequency of the recent history of syphilis. The interest of this investigation at the present moment lies in the fact that *in* 17 *out of* 19 *consecutive cases there was either syphilis or senile degeneration, the two most potent factors in the causation of thrombosis of arteries.* With regard to specific infectious diseases as a cause of acute myelitis, the number of such cases is very small, and, as Dr. Frederick Taylor points out, the recorded instances may very possibly include some of peripheral neuritis. Yet even if we allow that some are genuine, as they probably are, it is quite conceivable that thrombosis may occur as a result of the degenerative changes in the vessel walls which are known to be a result of the circulation of such toxins in the blood, while it is also possible that some are due to an actual inflammation of the spinal cord, the existence of which I am in no way prepared to deny.

A brief reference may be made to the close resemblance between the clinical pictures of cerebral thrombosis and the disease known as acute myelitis, a feature recognised for many years, and emphasised by Bastian in 1882. In both we have the occurrence, for a longer or shorter time, in many instances, of premonitory symptoms of a subjective nature, followed by a rapid onset, in from a few hours to two or three days, of the typical symptoms of the disease. In both, these symptoms frequently appear during the night, or when the individual is at rest in bed for some other reason; that is to say, when the circulation is at its slowest. In both we see a slow improvement up to a certain point, and the occasional occurrence of a second and even third attack in a different anatomical position. In addition may be stated the well-known clinical fact that not very infrequently a paraplegia supervenes in a patient suffering from hemiplegia of vascular origin.

The foregoing material may be briefly summed up as follows:—(1) So-called acute myelitis is found on microscopic examination, in the majority of recorded cases, to be not inflammatory, but due to thrombosis of spinal vessels. (2) That by far the most common cause of this thrombosis is syphilitic arteritis; and that senile arterial degeneration forms a considerable proportion of the remaining cases. (3) This view as to the pathology is confirmed clinically by the analogy between this disease and cerebral thrombosis.

In conclusion, I would urge that the recognition of thrombosis of spinal vessels as the most common cause of the symptom-complex described as acute myelitis is not merely of academic interest, but may be of practical value. It is possible that prompt treatment, in cases presenting premonitory symptoms and giving a history of recent syphilis, may ward off an attack of this nature. For this reason alone, to say nothing of the confusion which has arisen from the indiscriminate use of the term "myelitis," I submit that the nomenclature used by Dr. Bastian should be adopted, and that these cases be classed as "thrombotic softening of the spinal cord," or, more simply, "spinal thrombosis"—a name which at once suggests the analogy with cerebral thrombosis.

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DESCRIPTION OF FIGURES.

Fig. 1—Section through the margin of the softened area in the anterior column of Case 1, showing gross disease of the vessel-wall, with infiltration of its sheath with small round cells. Note the absence of leucocytal infiltration in the surrounding tissue.

Fig. 2.—Section from the margin of the softened area in Case 1, at a spot close to that of the preceding photograph, showing some completely occluded vessels and extravasation of red blood cells, but no leucocytal infiltration.

Fig. 3.—Section through the level of the lesion in Case 1, showing the small-celled infiltration limited to the perivascular sheath.

Fig. 4.—Section through the cord of Case 1 at the fifth cervical segment, above the level of the lesion, showing inflammation and thickening of the coats of the postero-median artery. Marchi staining at this level showed pure ascending degenerations.

Fig. 5.—Section through the lesion in Case 2, showing gross disease in the walls of the capillaries

Fig. 6.—Section through the lesion in Case 2, showing the great thickening about the postero-median vessels. Note the absence of small-celled infiltration in the surrounding tissues.

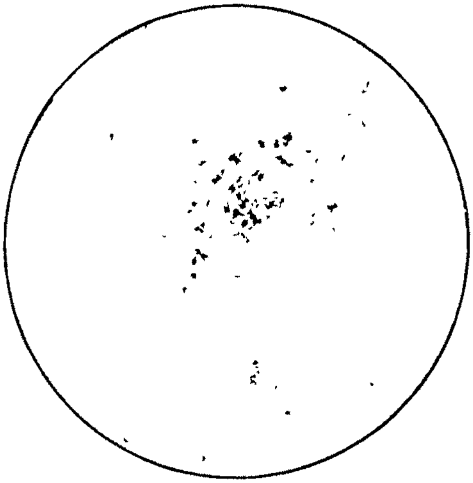

Fig. 1

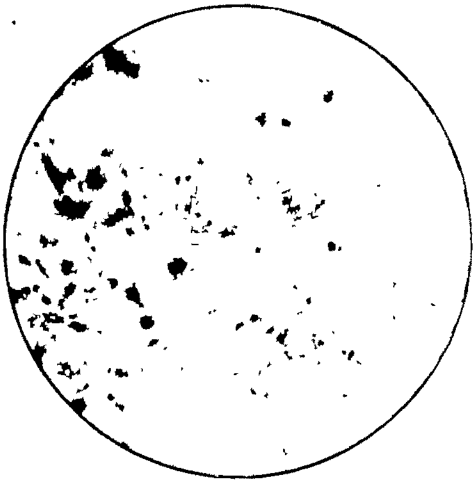

Fig. 2

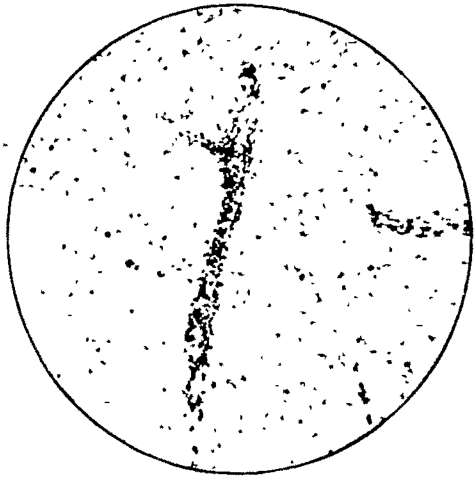

Fig. 3.

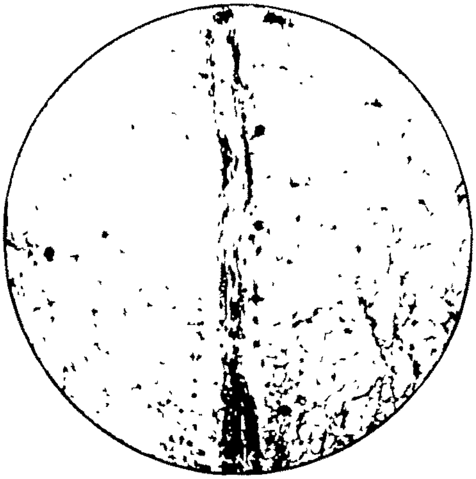

Fig 4.

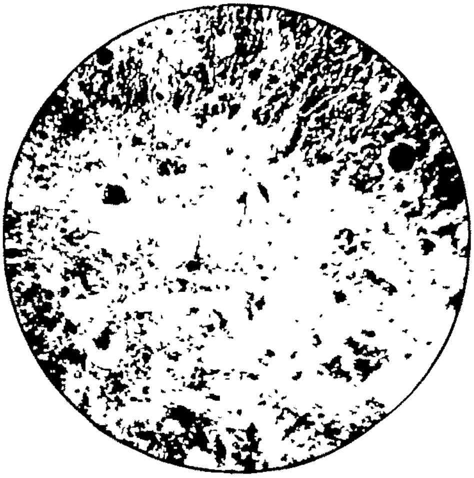

Fig. 5.

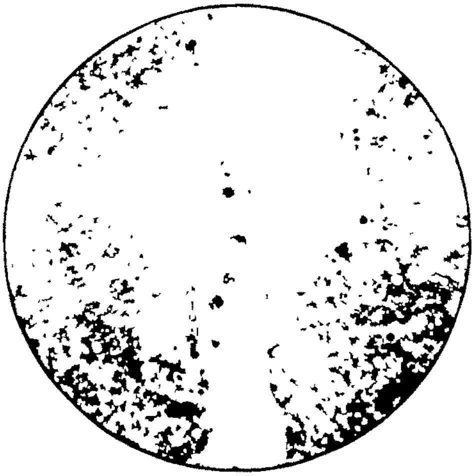

Fig. 6

A CASE OF ACROMEGALY UNDER OBSERVATION FOR FIVE YEARS, WITH CHARTS OF THE FIELDS OF VISION.

BY F. RICHARDSON CROSS.

Surgeon to the Bristol Eye Hospital.

Mr. W. H. B., aged 23, first consulted me on April 27, 1895, because his sight was becoming defective, especially for distance. I noticed that he had rather a large face and limbs, but I made no special investigations then, as he said his health was unusually good, that he had been playing in first-class cricket all the previous summer and keeping wicket without effort. His weight was 14 stone 7 lbs. The sight of the right eye was perfect for reading and good for distance— 3 D gave $\frac{6}{6}$. The visual field was perfect. The left eye saw only 2 J and ^{c}—3.5 D $\frac{6}{24}$, and the perimeter showed a "positive scotoma" in the upper part of the temporal field. Both optic nerves were pale, apparently to an equal degree.

On May 27, left vision had improved to—3 $\frac{6}{18}$ and the scotoma was much reduced.

The patient did not return again until May 17, 1897. He was then working in an office, and complained that his left eye had become blind and that the sight of the right was also defective. In the left eye there was barely perception of light, and that only in a limited portion of the upper temporal field (Chart 1). The visual field of the right eye was entirely lost on the temporal side (Chart 2); it was retained on the nasal side and at the fixation point, but central vision was reduced to—3·50 $\frac{6}{18}$. The eyeballs were normal in appearance, with no exophthalmos. Both optic nerves were white, the central retinal vessels of full size. There was no evidence of neuritis or of venous congestion. The patient was feeling ill, with loss of strength and pains in the limbs; he was troubled with headaches; his weight had gone up to 16 stone 7 lbs. His face was enlarged, and showed marked thickening of the orbital borders, prominent cheek bones, swollen lips, a much enlarged underhanging lower jaw, hypertrophied tongue, general thickening of the hyoid, thyroid and cricoid cartilages, enlargement of the clavicles, and thickening at the junction of the manubrium sterni with the body of that bone and with the cartilage of the second rib. His hair was very plentiful and coarse. He was very liable to free perspiration on any even moderate exercise.

The hands, wrists and feet were enormously widened and padded. The patellæ felt unusually developed. The external occipital protuberance and spinous processes of the cervical vertebræ seemed enlarged. He had lately been obliged to wear a larger hat and larger gloves and boots. It was evident that he was suffering from all the usual symptoms of acromegaly, and I sent him on for further advice to Dr. Michell Clarke, who on May 18, 1897, made the following notes :—

"W. H. B., aged 25½ years, grocer.

"Complains of failure of sight, of irritation from piles, of pains in the left side of head, and sometimes in the right side, worse at night. He feels weak, is disinclined for exertion, and easily tired. He is short of breath, and suffers from indigestion. His head is not so clear nor his memory so good as formerly ; he used to be very good at mental arithmetic, but has fallen off in this respect lately.

"He has been a good wicket-keeper at cricket, and could take fast bowling without gloves. (Probably his proficiency in this was due to the large size and some insensibility of the hands.) Lately the failure of sight has obliged him to give up cricket.

"He has never had any bad illness, and has never had syphilis. He comes of a healthy family ; his father suffers somewhat from rheumatism. His mother, one brother and three sisters are healthy. His maternal grandfather is said to have exactly resembled the patient in face and build, but was healthy, and died at 80 years of age.

"On examination the patient is a very big man, looks healthy, and is not anæmic ; six feet in height, with a large head, massive heavy thorax, and long arms ; the trunk is long, the pelvis rather small in proportion, the legs are short and bowed at the knees. The head measures 24½ inches in circumference. The face slightly prognathous. The face is a long oval, and is obviously enlarged, especially in its lower part, from increase in size of the jaw-bones, and especially of the lower jaw. The teeth are separated from each other, and those of the lower jaw lie outside those of the upper jaw all the way round, the front teeth of the lower being a quarter of an inch in front of the upper when the mouth is closed. The eyebrows and superciliary ridges are also large and prominent, but the forehead is otherwise not large. The ears are not enlarged.

"The tongue is enormous, flabby, and covered with a thick fur. The uvula and soft palate are also large, but the posterior end of the hard palate does not seem increased in size.

"The speech is nasal, thick, and deliberate; he speaks as if his tongue is too large for his mouth. Swallowing, hearing, smell, and taste are unaffected.

"No excess of subcutaneous fat over trunk; skin harsh and dry.

"Thoracic cage massive, deep, and powerful; measures 42½ inches in circumference. Clavicles large, 7½ inches in length; the thyroid and hyoid cartilages also appear to be enlarged. Thyroid gland can be felt, but is not increased in size. No dulness behind first piece of sternum (absence of persistent thymus). The scapulæ and scapular muscles seem large and prominent, and muscles of shoulder and arm are all large and extremely developed.

"Hands enormous, with well-marked ulnar pads; fingers large and 'sausage-like'; nails broad and large. Circumference of hands 11 inches. Huge bony wrists. Forearm and arm not large—former measures 12 inches round at thickest part. Lungs normal; heart normal. Abdomen and abdominal organs normal.

"The pelvis is not enlarged, nor are the muscles of the buttocks; the hamstring muscles are strongly developed.

"Legs show marked bow-legged deformity; knees not enlarged. Legs rather small in proportion.

"The feet are decidedly enlarged. This is noticeable as regards the soft parts, and perhaps also of the bones, but the feet are relatively not so large as the hands. Toes long; great toe shows especial enlargement. Foot measures 11 inches in length and 10½ inches in circumference. Penis and testicles not abnormal in size.

"No affection of motion or sensation (latter tested to touch, pain, and temperature) anywhere.

"Knee-jerks active. No clonus—superficial reflexes normal. All movements are slow and deliberate, like those of a big, heavy man, but otherwise normally performed.

"Mental state apparently normal; is a very intelligent man."

He now entirely rested from work, and was ordered thyroid tabloids (each representing five grains of the fresh gland), two daily, later increased to three daily. He also took thymus gland from the butcher.

He soon began to improve. His headache lessened, his sight gradually got better. In August he was ordered two pituitary gland tabloids and one thyroid daily, and in January three pituitary and two thyroid.

In February, 1898, his weight was reduced to 13 stone 8 lbs. The vision of his right eye was –3.50 $\frac{6}{18}$. The nasal side of the optic nerve was becoming pink.

Dr. Clarke, on February 24, 1898, says:—

"He feels on the whole better. He can ride a bicycle twenty to thirty miles, and his sight has so much improved that he can ride it through the town without difficulty. He could not have done this in August last. He feels more inclined for exertion, and is better in his head. The nocturnal emissions from which he suffered have ceased, and his digestion has improved.

"He is stronger on the legs, and has gained generally in muscular strength.

"I noticed the knuckles in his hands could be more plainly seen, and that the feet were apparently smaller. In other respects the conditions were unchanged; and I should like to make it clear that apart from the eyes, the muscular weakness, and slight mental changes which he himself described, I found at no time any evidence of disease of the nervous system."

July 27, 1898.—Weight 13 stone 7 lbs. Face appears smaller. Wears hat No. 7 instead of 7½. Feet require boots two sizes smaller. He can again wear pumps he wore at 19 years of age. He has left off elastic stockings for varicose veins of the legs, first worn when his sight became affected in 1895. He says his hands are certainly smaller. His sight improves; the right eye is not complained of; with the left eye he can distinguish pictures, furniture, and colours in the seeing field. The tabloids are causing headache, which diminished when they were reduced to one each daily of thyroid and pituitary. He felt as if he could resume work, but he only undertook some irregular writing.

May, 1899.—The patient is very much stronger. The sight of the eyes is improving. If taken with a large test object (a piece of paper 3cm. square), the field of the right eye is quite full, that of the left still defective on the nasal side (Charts 15 and 16).

In February, 1900, he was well enough to take a good-sized hotel, which he still has.

October, 1900.—The field of each eye is full to the 3cm. large white object, and Charts 17 and 18 show that, testing by the 5mm. pin-head, there remained only a slight crescent of *blindness* in the right field of both eyes, although vision was *dull* all over the right half of both fields.

After this date the patient considered himself so nearly cured that he ceased to attend. He had been treated almost regularly with thyroid and pituitary tabloids for upwards of three years.

Last February I asked the patient to come and see me. He was in excellent health, and doing his work without effort.

Side by side with progressive improvement in general health, there has been an easily demonstrable improvement in vision.

The left eye, from having been, on May 18, 1897, very nearly blind to light, now counts fingers readily at three feet; while the central vision of the right eye, once reduced to $\frac{6}{24}$ when corrected with myopic lenses, is now practically perfect with lenses.

Both optic nerves have been throughout anæmic and atrophied, and have shown no tendency to neuritis or to venous congestion. They are still very pallid, but the nasal side of the right now shows considerable normal vascularity, and even the left is becoming reddened and is likely still further to improve, although probably some of its nerve fibres are permanently destroyed.

A study of the Charts of the Fields of Vision suggests that there has existed considerable pressure on the optic nerve tract, which has paralysed the function of the compressed nerve-fibres, and that as the pressure has progressively diminished under treatment, the function of the implicated fibres has been restored or improved.

In several cases of acromegaly there have existed bitemporal hemianopsia, caused, as is supposed, by pressure of the enlarged pituitary body upon the optic chiasma. For in nearly all cases of the disease examined *post mortem*, some 36 in number, enlargement of the pituitary has been present, and the commissure of the optic nerves has been usually flattened over it.

In the case now under consideration, the impairment of the visual fields is essentially a right-sided hemianopsia, indicating pressure on the fibres of the left optic nerve tract; but besides this the fibres of the left optic nerve are more widely involved, either directly, or more probably through complication of the chiasma.

The defects in sight could be accounted for by a swelling of the pituitary body pressing on the left optic nerve tract just behind the chiasma, but implicating also those fibres of the chiasma which pass from the right optic nerve tract to the left optic nerve.

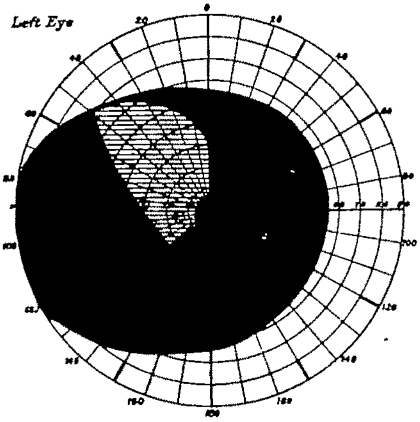

CHART 1.

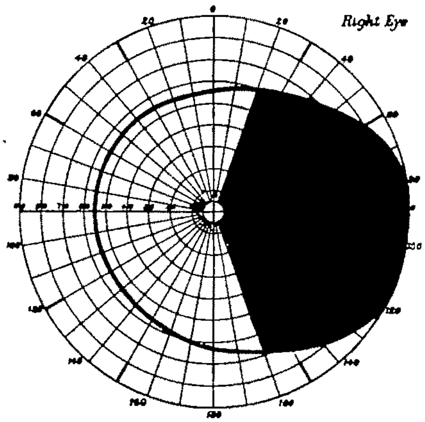

CHART 2.

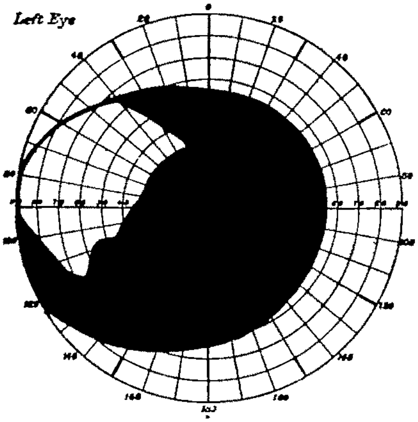

CHART 3.

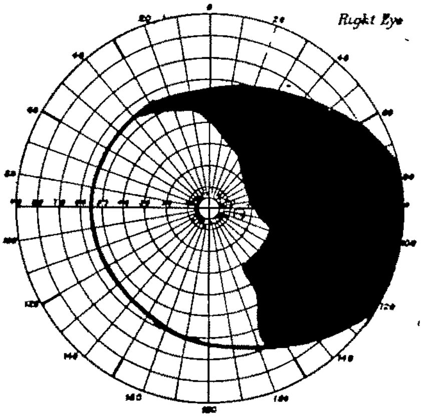

CHART 4.

It would seem that these latter more anterior fibres in the chiasma were first relieved from pressure; while the most permanently blinded area, that of the temporal side of the left retina, indicates that the outermost portion of the left optic nerve or nerve tract has been that most seriously and permanently damaged.

A series of Charts of the Fields of Vision, taken over a period of seven years,[1] show that in 1895 no definite serious impairment of sight was present, and the region implicated was quite different from that affected later. The condition of acromegaly was not then well pronounced.

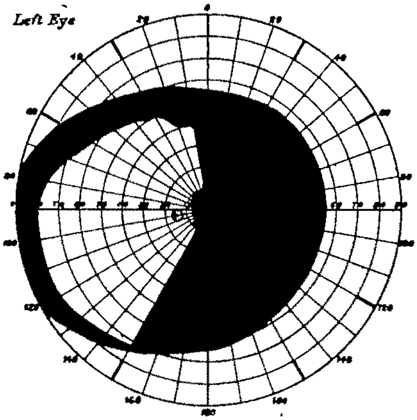

CHART 13.

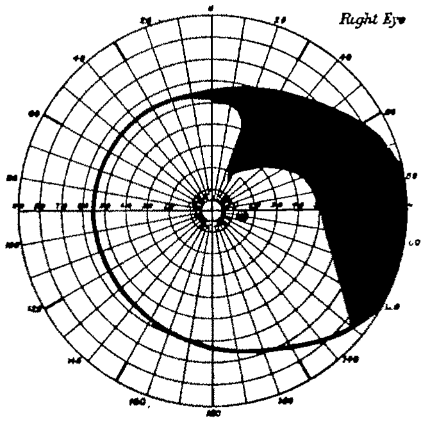

CHART 14.

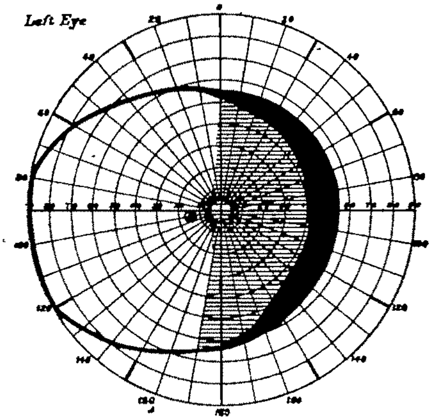

CHART 17.

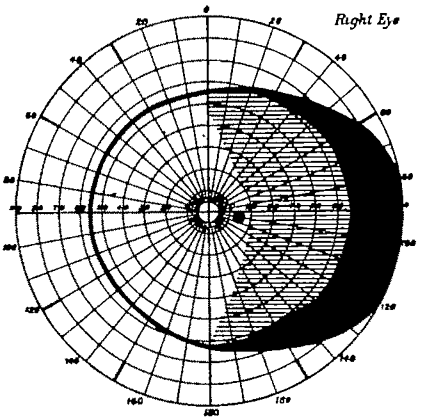

CHART 18.

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[1] Eight out of the 24 charts used to illustrate the paper are published herewith.

When the disease was definitely established in 1897 there was blindness in the temporal field of the right eye, and almost complete loss of sight in the left eye. The degrees of the blind portions in the visual fields of both eyes have progressively lessened with improvement in the general health.

With the exception of Charts 15 and 16, to which allusion has already been made as taken by a large test object, the series can be used for purposes of comparison. The fields were taken by means of a white pin-head 5 mm. in diameter.

At first the left eye could not recognise any object, and Chart 1 had to be taken by a candle flame; Chart 3 was taken by a test object 1 cm. square at a time when the smaller pin-head was not recognisable, but all the later fields of the left eye, and those of the right throughout, were taken with a 5 mm. white pin-head.

Compare Charts 1 and 2 with 3 and 4, at an interval of six months, and then after an interval of a year with 13 and 14, and after another year's interval with 17 and 18.

The charts taken in February, 1902, show that some deterioration has occurred in the power of the left eye since treatment had been partially discontinued for fifteen months. The patient is particularly well, and works hard in his hotel. No office has made any difficulty in passing him for insurance; he is insured in three offices as a first-rate life. There has never been anything the matter with his urine.

Review.

Experimental Psychology—Student's Manual, and Experimental Psychology—Instructor's Manual. By EDWARD BRADFORD TITCHENER. (Macmillan & Co., Ltd., London, 1901.)

THE author, in his preface to the Instructor's Manual, tells us that the object of these books in twofold. In the first place that "psychology is above the laboratory": that "we employ our instruments of precision, not for their own sake, but solely because they help us to a refined and more accurate introspection," and in the second place states that he has "treated the selected experiments, not as separate exercises, but as points of departure for systematic discussion." The two books must be taken together. In the Student's Manual questions are asked and exercises given, and the answers are fully gone into in the Instructor's Manual. It is unfortunate that the author does not make this clear to begin with, for the student is apt to be disconcerted by finding his book interspersed with abstruse questions, the answers to which are apparently nowhere to be found. In each volume there is an excellent introduction, which deals with methods. The introduction in the Student's Manual is devoted to giving the pupil much valuable advice on the manner in which experimental work should be conducted. The "Hints to the Instructor" in the introduction to the Instructor's Manual are in every way admirable. The author insists on thoroughness, and rightly points out the "utter uselessness of experiments, such as reaction times, without the accompanying analyses of the action-consciousness." The author divides the books into two parts. In the first part he deals with sensation, affection, attention and action; the second part is devoted to perception, idea, and association of ideas. Both volumes are well illustrated with figures of all the important experiments. At the end of the Instructor's Manual will be found a number of examination questions. The author has evidently devoted much care to the index in each manual. In works of this kind it is all-important to have a very full index, and in this respect no fault can be found with these manuals. These books are published at an opportune time, and will certainly supply a want for those anxious to work at experimental psychology. Throughout these manuals the author conveys to the student that he is not the exponent of a new psychology, but shows that for really valuable psychological research we must have experimental work in addition to purely introspective study. An experiment may modify, to a certain extent, an action, but the advantages gained by standard experiments more than outweigh the disadvantages. The purely introspective psychology is too diffuse, the personal equation is too large a factor. Experimental work tends to make us more accurate and our research more scientific. We strongly recommend all students of psychology to carefully study these books. The subject-matter is clearly and tersely put, and the author has succeeded in compressing into a comparatively small space an enormous amount of work.

MAURICE CRAIG.

PROCEEDINGS OF THE NEUROLOGICAL SOCIETY OF LONDON.

AT the CLINICAL MEETING held at 11, Chandos Street, on Thursday, May 22, 1902, at 8.30 p.m., the following cases were shown:—

Dr. F. J. SMITH.—*Boy with paresis of right side.*

Ernest D., aged 9, admitted March 15. Mother states that the child was quite well eight months ago. First noticed weakness of hand of boy, and that he could not hold a pen. This weakness has increased gradually, but more rapidly just previously to his being sent to hospital. No history of any fits. No family history bearing on case. Lost right eye result of accident two years back.

The labour at birth of this child was prolonged and difficult. Instruments were used.

Heart and lungs normal on examination. Intelligence good.

Cranial nerves.—Left fundus normal. No external ocular paralysis. No inequality of movement of sides of face. No speech defect. Tongue protruded straight.

Sensation.—Patient could not recognise heat and cold on right side of limbs and trunk, but could do so on right side of face. Right arm rigid, and not used voluntarily. Left arm normal. Right leg rigid, not wasted.

Reflexes.—Arm glib, especially right side. Right knee-jerk increased. Right ankle clonus obtained. Left knee-jerk present. No ankle clonus.

Mr. F. RICHARDSON CROSS.—*A case of acromegaly under observation for five years, with charts of the fields of vision.*

Mr. W. H. B., aged 30, a strong, intelligent man, a licensed victualler, showing the typical characteristics of acromegaly.

The *cranium* was rather large, but apparently normal. The *face* showed marked thickening of the borders of the orbits, prominent cheek-bones, and a much hypertrophied "underhung" lower jaw. The lips were swollen and the tongue enlarged, as the palate also seemed to be. There was some general thickening of the hyoid bone, and of the thyroid and cricoid cartilages. The clavicles were large, especially the right one, and there was swelling at the junction of the manubrium with the body of the sternum, and at their attachment with the second rib cartilage.

The spine and pelvis were normal. The spinous processes of the cervical vertebræ were large. No exostoses were present in any parts of the bony skeleton. The knees were bowed outwards —the upper ends of the fibulæ enlarged, and the patellæ unusually developed. The hands and fingers were typically massive, but not lengthened. There was marked enlargement of the lower end of the radius. The feet were heavy, flat and broad, the metatarsal bones seemed normal, but the tuberosity of the os calcis was hypertrophied.

The patient when shown was wearing smaller boots than he did some little time previously, and his hands were also getting smaller. His weight had diminished 3 stones under treatment. The sight was good in the right eye (J1—3$\frac{6}{8}$), but the field of vision was not quite perfect on the temporal side. The optic nerve was very pale. The left eye, at one time almost completely blind, showed well-marked atrophy of the optic nerve, but with it he could count fingers at three feet, and vision was improving.

The series of charts shown well illustrated the gradual improvement of vision under treatment, and the relief of pressure on the visual tract.

The case was essentially one of right-sided hemianopsia, indicating pressure on the left optic tract, but the fibres of the left optic nerve were more widely involved.

The swelling of the pituitary body had probably pressed chiefly on the left optic nerve tract, just behind the chiasma, implicating also the fibres in the chiasma close to the left optic nerve. But the more permanent blindness of the temporal side of the left retina indicated that the main pressure had been upon the outermost portion of the left optic nerve tract.

Treatment.—Tabloids of pituitary body, of thyroid and thymus, and thymus gland from the butcher.

Dr. W. S. Colman.—*Case of Symmetrical Paralysis of Acute Onset involving the Deltoid and other Muscles round the Shoulder-joint.*

Arthur E., aged 39, previous health good. No history of syphilis. Not exposed to lead. Was vaccinated on March 20, 1902; the vesicles developing well, with little surrounding inflammation. On April 11 complained of pain and stiffness in both shoulders. Next day, on waking, found that he could not raise his arms. The pain, though much less severe, had not subsided.

On examination, there was wasting and loss of power in the muscles round both shoulder-joints. The loss of power was almost complete in the deltoids and external rotators of the arm and the clavicular part of the pectoralis major, less marked in the triceps, biceps, lower part of the pectoralis major, and in the pronator radii teres. The deltoid did not react to Faradism, and gave a well-marked reaction of degeneration. The other muscles mentioned reacted to Faradism, though feebly, and their response to galvanism was sluggish, but there was no polar change. No fibrillary tremors. Forearms and hands normal.

Sensation.—Common sensation was perfect. Sensation to pain preserved, except over a small area near the insertion of the deltoid. Faradic sensation was lost over the whole of the deltoid, but was keen elsewhere. There was almost constant aching pain. No herpetic eruption. Knee-jerks brisk. No ankle clonus. Plantar reflex; flexor response. No affection of sphincters.

The paralysis was regarded as due to some affection of the cord formed by the union of 5th and 6th cervical roots, possibly toxic, and connected with his re-vaccination.

Dr. PARKES WEBER.—*Case of Meralgia Paræsthetica after Vaccination.*

G. H., aged 55, a somewhat obese man, with a tendency to varicose veins of the lower extremities. He has not suffered from any serious illness, except from pneumonia in 1870 and from malignant pustule (anthrax) of the right arm in 1866. No history of syphilis or alcoholism. During last March he was vaccinated on the left arm, and very considerable swelling and suppuration followed. About two weeks after the vaccination, at a time when his arm was very bad, he first noticed the disagreeable sensations in the outer and front part of the right thigh, from which he at present suffers. These sensations are described as numbness and drawing together of the skin, and often actual pain. A disagreeable feeling is continually present, but the pains ("meralgic paroxysms") only occur now and then. There is no real anæsthesia, but the feelings produced by contact of objects with the skin are abnormal, and quite different to those experienced over the rest of the body. Thus great discomfort is occasioned by keys or similar objects in the trousers pocket of the affected side. The paræsthetic area, which extends downwards to about an inch above the patella, corresponds fairly well to the skin normally supplied by the external cutaneous nerve of the thigh. On inspection it does not differ at present from the corresponding part on the other thigh, but a week or two ago it is said to have presented a certain degree of swelling and redness. Sensation has been tested by sharp points and blunt objects, and by the application of ice, hot water, &c. Over the affected area there is marked hyperæsthesia for ordinary touch, pressure, pain, heat and cold, and likewise for Faradic stimulation. In regard to the general condition of the patient nothing abnormal has been detected beyond a certain amount of obesity and slight varicose veins in the lower extremities. There is nothing in the pupillary reflexes or knee-jerks, or anything else, to give rise to a suspicion of tabes dorsalis. Urine: specific gravity 1020, clear, acid, no albumen, no sugar. It is important, however, to mention that during the last four years a truss has had to be worn for right inguinal hernia. The present truss has been used for the last half-year. Owing to his work as gatekeeper and porter, the patient has to be nearly the whole of the day standing or walking about.

This affection, which is probably not very rare, was described in 1895 by Dr. Martin Bernhardt, of Berlin (*Neurologisches Centralblatt*, Leipzig, 1895, page 242), as a paræsthesia of the nervus cutaneus femoris externus, and about two weeks later by W. K. Roth, in Moscow (abstract in *Revue neurologique*, Paris, 1895, page 668), as "Meralgia paræsthetica" (*μηρός*—thigh). Since then various writers have referred to it and described cases. The symptoms in the present case seem not to be aggravated by mere walking exercise, as some patients have described them to be, but the sensitiveness of the skin to pressure resembles that in the officers, referred to by Bernhardt, who found the pressure and movement of the sword against the thigh almost insupportable. Nearly all the patients have been males of the middle period of life, and the disturbance of sensation has generally been confined to the area supplied by the external cutaneous nerve of one thigh. Sometimes, however, it has been bilateral; occasionally it has occurred in women, and in one or two cases the paræsthesia has extended beyond the limits of the area normally supplied by the external cutaneous nerve. Although the symptoms somewhat resemble the local paræsthesiæ met with in tabes dorsalis, the affection appears not to be connected with any spinal cord disease. It remains a localised condition, and is of no serious import, but the discomfort and continual annoyance caused to the patient may equal those produced by the paræsthesiæ of tabes. They have in some cases justified the resection of a portion of the external cutaneous nerve from the upper part of the thigh, after treatment by the Faradic brush, baths, massage, &c., have failed. Satisfactory results have been recorded from this little operation. In one or two instances a part of the nerve removed from near the anterior superior iliac spine has been found to show a nodular fibrotic change (*cf.* Dr. E. Nawratzki, *Deut. Zeitschr. für Nervenheilkunde*, 1900, vol. 17, page 99). The affection has been attributed to infectious diseases, such as enteric fever, lead poisoning, and local traumatisms. In the present case obesity perhaps acted as a predisposing cause, as it doubtless does for various forms of neuritis, but the exciting agents probably were (1) some local chronic irritation or traumatism to the nerve trunk, either from the truss or from the stretching of the fascia lata of the thigh caused by the patient's occupation obliging him to keep on his feet for so long a time every day, and (2) a toxæmic condition from the severe suppurative inflammation after vaccination.

Dr. E. FARQUHAR BUZZARD.—*Myasthenia Gravis.*

F. H., Factory hand, aged 18, after some mental worry two years ago, suddenly experienced difficulty in articulation and in movements of tongue. Some months later noticed inability to close eyes properly. Became easily tired by walking, and his arms failed quickly when hammering. *Present condition*: Well-nourished lad, with no wasting of muscles. Almost permanent palsy of orbiculares, palpebrarum and iris, and of occipitofrontalis. No ptosis. Facial movements weak and variable. Tongue and palate movements weak and easily exhausted. Arms strong, but exhausted more easily than normal. Back muscles easily tired.

Reflex and sensory conditions normal.

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BRAIN.

PART III., 1902.

Original Articles and Clinical Cases.

DEGENERATIONS FOLLOWING LESIONS OF THE RETINA IN MONKEYS.

BY J. HERBERT PARSONS, B.S., B.Sc., F.R.C.S.

Curator, Royal London (Moorfields) Ophthalmic Hospital; British Medical Research Scholar.

(From the Physiological Laboratory, University College, London, and the Pathological Laboratory, Royal London Ophthalmic Hospital).

THE optic nerve, so-called, consists of centripetal and centrifrugal fibres, of which the former are probably the more numerous. Of these, most are believed to be the axons of the ganglion-cells in the retina. If therefore, groups of the ganglion-cells are destroyed, we should expect to find the corresponding fibres of the optic nerve degenerated, and to be able to trace these fibres to their ultimate destinations in the brain. This line of research has hitherto received very scanty attention.

Falchi (1) in 1886, and Baquis (2) in 1889, made retinal lesions for the purpose of studying the reaction of the different retinal elements.

Pick (3) in 1895, destroyed circumscribed areas of the retina in a very large number of rabbits, and traced the degenerations in the optic nerves, chiasma and tracts. He arrived at the following conclusions:—"The fibres retain, throughout their whole course, both in the optic nerve and in the optic tract, the same relative position; the crossing in the chiasma occurs in regular sequence: first the innermost bundles of the optic nerve, and then successively those lying farther outwards; definite parts of the transverse section of the optic nerve thus correspond to definite parts of the tract of the opposite side. To the lower parts of the optic nerve answer similarly the parts lying below in the tract; to the inner parts of the optic nerve, the outer parts of the tract; to the outer parts of the optic nerve, the inner parts of the tract; as also it is probable that the upper parts of the tract correspond to the upper part of the nerve. In the chiasma, there is merely a decussation of fibres in the transverse direction, and not any rearrangement of them in the vertical direction. The topographical relations between the retina and the optic nerve can be defined thus:—The different parts of the optic nerve correspond in general to the similarly situated parts of the retina; and in a similar manner, the relations between the retina and tract of the contralateral side are in accordance with the same arrangement."

As in the earlier researches of von Gudden, the small direct tract which exists in the rabbit seems to have escaped Pick's observation. Pick made one or two observations upon cats, with the same results.

Dean and Usher (4), independently, in the same year, arrived at similar conclusions with regard to the optic nerve in rabbits. They do not record any investigations of the chiasma or tracts. They also made a lesion between the disc and the macula in a monkey, and obtained degeneration in the papillo-macular bundle in the optic nerve. The degeneration was similar in distribution to that found in cases of toxic amblyopia, viz., a wedge-shaped area on the temporal side near the eye, becoming crescentic and nearer the centre of the nerve farther back, and finally central near the chiasma.

METHOD.

In my experiments operations were performed upon six monkeys. The pupils having been previously well dilated by the instillation of atropine, the animal was anæsthetised with ether. The fundus was examined ophthalmoscopically to see that it was normal, and the conjunctival sac was washed out with weak solution of perchloride of mercury. A speculum was inserted, and the eye fixed by fixation-forceps, held by an assistant. A Graefe's cataract knife was then introduced into the eye 4 or 5 mm. behind the corneo-scleral margin, at either the nasal or temporal side, thus avoiding dangerous injury to the ciliary body, and minimising injury to the retina. The knife was passed across the eye through the vitreous to the opposite side, and the retina wounded there to the required extent, the position of the point of the knife being in some cases observed by the ophthalmoscope (direct method). The ophthalmoscope was especially used in lesions near the disc or macula. In other cases, the wound was made without ophthalmoscopic examination, the slight resistance encountered being sufficient to show that the retina had been reached. The exact position and nature of the wound were subsequently determined by ophthalmoscopic examination, which was repeated after an interval of a few days, and also shortly before killing the animal. The lesions were all investigated microscopically by a suitable section of the eye, *post mortem*, and were then prepared for microscopic examination. The results of the latter investigation have elicited several points which are of ophthalmological rather than neurological interest, and will be detailed elsewhere.

There was usually no loss of vitreous during the operation, but a small bead escaped in two cases, without, however, causing any untoward result. The wound of entrance healed with great rapidity in all cases. There was slight hyperæmia of the conjunctiva for a day or two, but this quickly passed off, and the animal looked perfectly normal.

The monkeys were chloroformed to death from a fortnight to three weeks after the injury. The brain was removed and placed in formol, the optic nerves being cut through immediately in front of the chiasma. The roofs of the orbits were then removed, and the optic nerves dissected free from the other orbital contents. Great care was taken to preserve the accurate orientation of the nerves. The eyes were left *in situ* until the orbits had been dissected back to the foramina, so that the nerves were thus anchored at each end. The eyes, with the nerves attached, were then lifted out of the orbits and pinned out upon a piece of cork. They were then hardened in formol. When hardening was completed, the eyes were removed and examined. The nerves were pinned out, side by side, upon a piece of liver, and transferred, after thorough washing in running water, to Busch's solution. In this condition they were put through the alcohols and embedded in celloidin, the pins being removed after the celloidin had set. Small, fine, entomological pins were used. There was usually a slight reduction of osmium around the pin-holes, but this did not extend for any distance into the nerve, and the degenerations were determined from careful examination of many sections, and not from isolated ones. The sections were cut with a Jung microtome, every fifth (in some places, *e.g.*, the chiasma, more) being mounted and examined.

EXPERIMENTS.

Experiment I.—Rhœsus. Right Eye.

October 16, 1901. A small lesion, about 2 mm. long, in a direction tangential to the disc, was made near the equator in the lower nasal quadrant. There was a little hæmorrhage; the area of pigmentary degeneration was very little larger than the lesion.

October 31, 1901. Killed.

The degenerations in the optic nerve are shown in the micro-photographs on Plate I. The degenerations in the optic nerve, chiasma and tracts are shown diagrammatically in figs. 1 to 8. (The outlines of the diagrams were all drawn with the Edinger Projection Apparatus, the details being filled in free-hand, under a higher power, only degenerations which could be traced along the nerve being drawn. The diagrams therefore represent what are believed to be the essential degenerations following the given lesion.)

Figs. 1 to 5 show that the main area of degeneration is wedge-shaped near the eye, the apex of the wedge being

PLATE I.

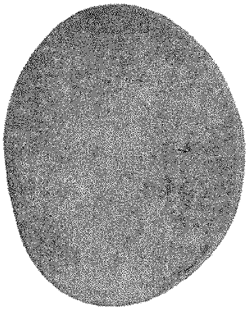


Fig. 1.

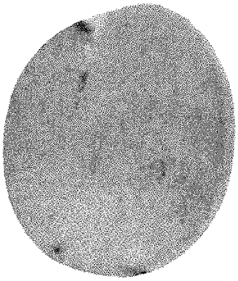


Fig. 2.

Fig. 3.

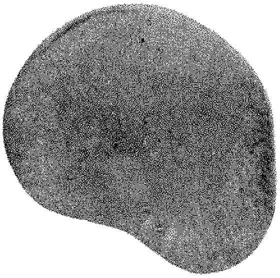


Fig. 4.

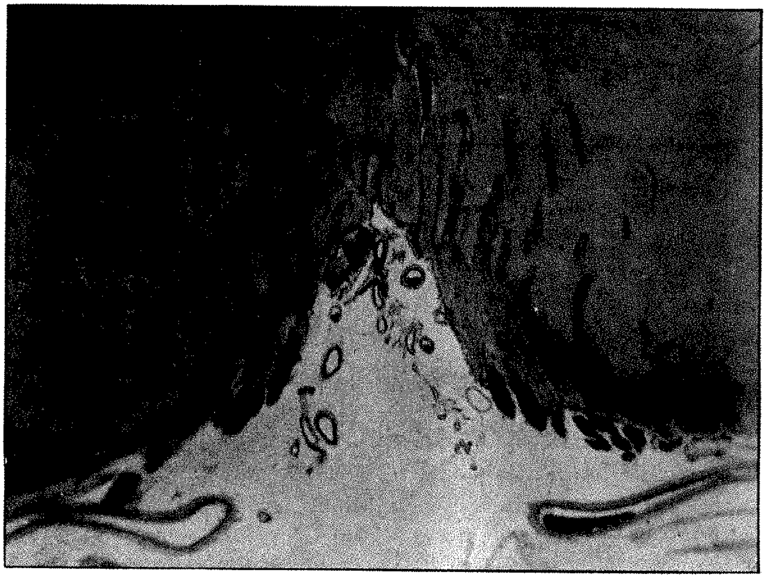
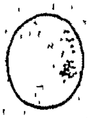


Fig. 5.

towards the centre of the nerve, and the base at the periphery, the whole lying in the upper part of the inferior nasal quadrant. There are scattered degenerated fibres over the whole nasal side, and a few isolated ones upon the temporal side. In sections taken more posteriorly, behind the entrance of the central retinal vessels, the shape of the area occupied by degenerated fibres becomes more crescentic, but is still nasal. Fig. 6 is a nearly vertical (frontal) section of the chiasma. It shows the fibres crossing, principally in the inferior or ventral part of the chiasma. Fig. 7 is a slightly more oblique section farther back, being in a direction downwards and forwards. The degeneration is therefore ventral and anterior. Fig. 8 is still more oblique, approaching the horizontal, so that only the extreme posterior part of the chiasma is shown, and the tracts are cut more or less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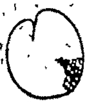
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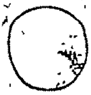
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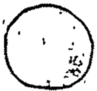
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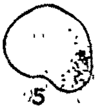
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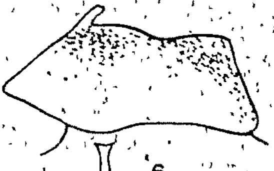
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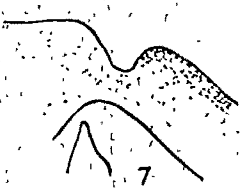
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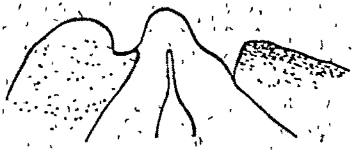
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longitudinally. Very few fine dots of degeneration are seen in the chiasma and tract of the same side, the main area of degeneration being in the outer part of the contra-lateral tract. Farther back the fibres spread out over a larger area of the section of the tract, becoming diffuse as they approach their termination.

In sections passing through the bundles of the third nerve as they leave the brain in this monkey, some apparent degeneration was seen on each side. The same occurred to a less extent in the decussation of the fourth nerves. The interpretation of this and other anomalies will be discussed later.

Experiment II.—Jew. Left Eye.

October 30, 1901. A rather larger lesion, about 3 mm. long, was made in a direction tangential to the disc a little in front of the equator in the lower temporal quadrant of the retina. There was practially no hæmorrhage, and the pigmentary degeneration was limited to the lesion.

November 18, 1901. Killed.

The degenerations in the optic nerve are shown in figs. 9 to 11.

Figs. 9, 10, and 11 show that the main area of degeneration is on the temporal side along the whole course of the nerve. It is most marked, and is very dense in the lower temporal quadrant, being more or less wedge-shaped near the eye, and becoming rounder farther back. It tends to become more dorsal near the chiasma, but it is possible that may be due to slight error in orientation. As in I., there is some diffuse generation, most marked on the temporal side. The fibres lie principally in the dorsal part of the chiasma. Many degenerated fibres are seen crossing to the opposite tract. Farther back the fibres lie principally in the central part of the tract of the same side. Posteriorly, they spread out and become more diffuse. In a similar area of the tract of the opposite side, *i.e.*, dorsally and centrally in front, becoming broader behind, there are many finer black spots of degeneration.

The areas including the third and fourth cranial nerves were not sectioned in this brain.

Experiment III.—Bonnet. Left Eye.

November 20, 1901. A very small lesion was made upon the temporal side near the equator, just below the horizontal meridian. There was no bleeding. Macroscopically there was only a white dot at the site of the lesion.

December 7, 1901. Killed.

The degenerations in the optic nerve are shown in figs. 12 to 14.

It will be seen that the degeneration is almost limited to the inferior temporal quadrant, and is very slight. In the chiasma it is at first ventral and anterior in position, gradually tending towards the dorsal surface. In the tract of the same side it is central and dorsal at first, becoming more diffuse posteriorly. There are only a few scattered fibres degenerated in the contra-lateral tract. There was apparent degeneration in the bundles of both third nerves.

Experiment IV.—Rhesus. Right Eye.

January 13, 1902. The lesion was larger, about 3 mm. long, in this retina. It was on the temporal side, a little behind the equator, and extended above and below the horizontal meridian. There was slight hæmorrhage, and, *post mortem*, there was an oval area of pigmentary degeneration, with axes of about 4 mm. by 3·5 mm. The retina was firmly adherent to the choroid over this area.

February 1, 1902. Killed.

Figs. 15 to 17 show the degenerations in the optic nerve. It is seen to be diffused over the whole temporal side of the nerve, without any special area of concentration. In the chiasma it occupies the central and dorsal parts. There is no degeneration in the ventral part. In the tract of the same side the degeneration is arranged much the same as in II., but more fibres are affected. There is a finer, scattered degeneration in the contra-lateral tract.

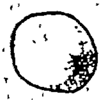
The third and fourth nerves were not cut.

Experiment V.—Rhæsus. Left Eye.

January 14, 1902. A small lesion was made between the macula and the disc, but at a slightly lower level. It was rather deep, injuring the choroid and sclera, and there was some hæmorrhage.

January 28, 1902. This monkey died in the morning; it was dissected about two hours afterwards.

Fig. 18 shows the distribution of the degeneration in the anterior part of the nerve. Posteriorly it became more central. It occupied the central part of the chiasma, and continued central, and rather dorsal in the anterior part of the same tract, becoming more diffuse posteriorly. There was a large amount of degeneration considering the small extent of the lesion. This was probably due to its proximity to the disc and its situation in the neighbourhood of the macula. There was fine degeneration in the contra-lateral tract, the fibres crossing in the central part of the chiasma.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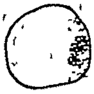
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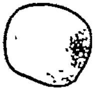
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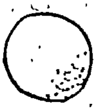
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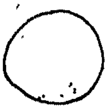
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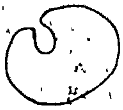
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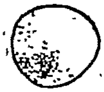
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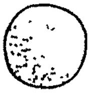
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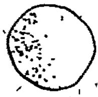
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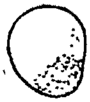
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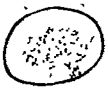
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There was apparent degeneration in the bundles of both third nerves.

Experiment VI.—Rhœsus. Left Eye.

January 25, 1902. A lesion, 2mm. long, was made in a direction down and out, starting 2mm. down and out from the fovea centralis. There was considerable hæmorrhage into the vitreous.

February 15, 1902. Killed.

Fig. 19 shows the distribution of the degeneration in the posterior part of the nerve.

In the anterior part of the nerve it is most marked on the temporal side, especially just below the horizontal; but there is also a considerable amount of degeneration over the whole area of the section. It is chiefly central in the anterior part of the chiasma; in the posterior part, where the sections are more oblique, *i.e.* about half way between vertical and horizontal, it occupies a crescentic area at the periphery of each side with a connecting band in front. In this situation, therefore, the degeneration tends to become dorsal and external. Farther back, at the commencement of the tracts, there is degeneration in the central, and slightly dorsal parts on each side; and this becomes diffused over the whole tract still more posteriorly.

There is apparent degeneration in the bundles of both third nerves (Plate I., fig. 5).

REMARKS.

(1) *The optic nerve on the side of the lesion.*—My experiments on the monkey agree, upon the whole, with the previous observations of Pick, and of Dean and Usher upon rabbits. They also afford some confirmation of the experiment of Dean and Usher upon a monkey, and of the results arrived at by pathological investigation of cases of toxic amblyopia, in which the papillo-macular bundle is particularly involved. [Samelsohn (5), Nettleship (6), Vossius (7), Uhthoff (8), &c. (9), and especially a very important case reported recently by Birch-Hirschfeld (10).]

Pick's statement, quoted above, holds good as a general conclusion, so far as it refers to the optic nerve. I have invariably found some diffuse degeneration, and this is scarcely to be wondered at. The lesion made by the point of a Graefe's knife is minimal, probably much less than by the point of a galvano-cautery. At the same time, in dealing with such a delicate structure as the retina, it is not surprising if the injury is not absolutely localised. It is only rarely possible to effect one's purpose without injury of the choroid or even the sclerotic, and it is impossible to entirely avoid the retinal vessels. A slight amount of hæmorrhage into the vitreous usually occurs, and the mere passage of the narrow knife across the eye must lead to reactive changes, probably accompanied by transient shrinking of the vitreous, which may well interfere with the nutrition of ganglion-cells in other parts of the retina.

As might also be expected, the nearer the lesion is to the optic disc, the greater is the resultant degeneration, for not only are the ganglion-cells destroyed, but the axons of ganglion-cells over a large peripheral area are also cut through. The experiments of Baquis and others afford no evidence of regeneration in these fibres, and as they belong strictly to the central nervous system, it is inherently improbable. Moreover, the time allowed is probably too short.

The very definite course of the macular fibres, which do not follow the law which Pick has stated, must cause some dislocation of the other temporal fibres; but the method is not sufficiently accurate to elucidate this point. It may possibly be settled in the future by pathological observations.

One slight modification of the general law as to the localisation of the fibres may be noted, viz., that in the posterior part of the nerve as it approaches the chiasma, the nasal fibres tend towards the ventral side, and the temporal fibres tend towards the dorsal side.

(2) *The optic nerve on the uninjured side.*—Both Pick and Dean and Usher, observed signs of degeneration in the nerve of the opposite—uninjured—side. This observation I am obliged to confirm. It may be mentioned at once that degeneration in my sections was limited to the visual paths, *i.e.*, there was no trace of it in other parts of the brain, actually forming parts of the sections, and therefore subjected to identically the same method of preparation.

PLATE II.

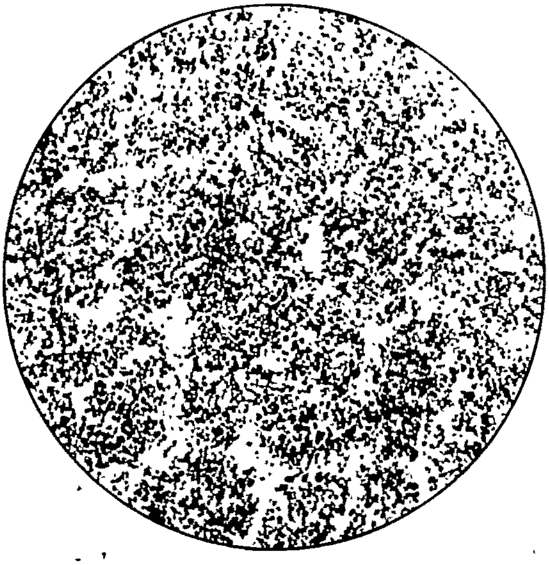

FIG. 1.

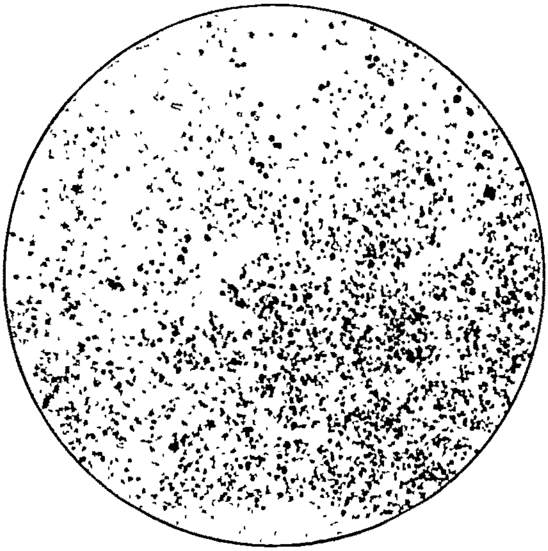

FIG. 2.

In all the specimens it was a diffuse degeneration, usually without very definite areas of concentration, and always considerably less than on the injured side. The degeneration could be traced throughout the length of the nerve, and such concentration of fibres as occurred retained its relative position in all the sections. As a rule this was on the homonymous side of the nerve, as compared with the side of the lesion. Thus in Experiments II., IV., and V., with temporal lesions, the degenerated fibres were principally upon the external sides in both nerves. In Experiment III., with a very small temporal lesion, there were very few degenerated fibres in the other nerve. In Experiment VI. the degeneration was diffuse. In Experiment I. it was also diffuse, but there were a good many degenerated fibres upon the outer side of this nerve, although the lesion was nasal.

I must confess to scepticism when reading of these degenerations in the papers of previous observers, which was only allayed when I found that it was a constant result in my own experiments. One is naturally led to doubt whether it is not due to some error in technique; but the earlier observations were made with the original Marchi method, and in my experiments all the degenerations were limited to visual paths. Professor Schäfer has pointed out the necessity of getting rid of all traces of formol before placing the specimens in the osmic acid mixture, and this I was careful to do by thorough washing in running water. That the appearances are exactly those of degenerations is shown by the illustrations under a high power in Plate II., one of which is taken from the nerve on the side of the lesion, and the other from the opposite nerve.

There is one pathological examination on record which affords some support to this result. Kellermann (11), in a case of old-standing atrophy of the left optic nerve, found a small tract of degeneration in the right nerve, ventro-lateral near the eye, becoming central near the chiasma, and therefore running in the course of the macular bundle. No abnormality of vision was noticed during life, and the central vessels entered the nerve at the inner and lower part (this is not invariable), so that the bundle ran independently of them. Kellermann attributes the degeneration to compression of the fibres in the chiasma, due to shrinking from atrophy of the fibres of the left nerve. Hebold (12), in a similar case, using Pal's method, found the nerve sound; but the method is not sufficiently sensitive for the purpose. Deutschmann (13), Henschen, and others have also been unable to demonstrate degeneration in pathological cases.

Kellermann's explanation of degeneration in the nerve of the uninjured side is very improbable; there is no evidence in its favour, and much of a general nature against it. Usher and Dean suggest that fat may be removed from the degenerated nerve and carried by lymphatics and deposited in the opposite nerve. This suggestion is equally far-fetched. We are forced to conclude that the degeneration is a genuine one, and, if so, what is the nature of the fibres involved? It is not probable, as Usher and Dean point out, that they are concerned in the pupillary reflexes, as these reflexes remain absolutely unimpaired. We are forced to conclude that they belong to some form of inter-retinal fibres—a reversion, in a sense, to the old inter-retinal tract (commissura arcuata anterior of Hannover, vordere Bogen commissur of Stilling). Ramon y Cajal (14) has demonstrated, by the methylene blue method in rabbits, a division of the optic fibres, and Kölliker discovered an isolated example in a human embryo. Bernheimer (15) was struck by the variety in the size of the fibres in the chiasma, so that it appears in many places as if the larger fibres divided. It is not improbable that the degenerated fibres in the nerve of the uninjured side are collaterals, and that they are distributed to physiologically corresponding parts of the opposite retina, possibly inducing chemical changes in the visual substances or movements in the cells, and so afferent impulses which subserve a modified type of binocular vision. This, however, must be left for further investigation.

(3) *The optic tracts.*—In all cases there was degeneration in both tracts. This may be explained partly by the diffuse injury which probably always results from the lesion, and which is manifested by diffuse degeneration in the nerve. I do not think that this accounts for it entirely. There are

apparently more fibres degenerated in the tracts than in the nerve, and we are here even more powerfully forced to the conclusion that division of the fibres occurs. Most of the experiments were purposely temporal lesions, in order, if possible, to obtain a pure degeneration in the homolateral tract. In these cases the degeneration in the contra-lateral tract usually showed smaller black globules, as if less myelin was present. Probably these were finer fibres—in fact, collaterals.

(4) *Apparent degeneration in third and fourth nerves.*—I do not think that this was a true degeneration, but an artefact similar to that obtained by Marchi in some of his early experiments.

The expenses of this research were defrayed by a grant from the Royal Society.

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(6) Nettleship. *Trans. Ophth. Soc.*, vol. i., 1882.

(7) Vossius. *Graefe's Archiv für Ophthalmologie*, Bd. xxviii., 3, S. 201, 1882.

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NOTE ON THE ARTERIAL SUPPLY OF THE BRAIN IN ANTHROPOID APES.

BY A. S. F. GRÜNBAUM, M.D., F.R.C.P.

AND

C. S. SHERRINGTON, M.A., M.D., F.R.S.

(Physiological Laboratory, Liverpool).

AMONG features of human character pertaining to the anthropoid apes we find one not hitherto recorded, namely, the existence in the cerebral arterial supply of a *Circulus Willisii* resembling that of man. In these highest apes, as in man, an interior communicating artery quite frequently completes the *circulus* in front. "In all the lower mammals," Mr. Parsons, who has recently examined the arrangement of the blood-vessels of the brain of a large number of mammalian forms, writes us, "which I have examined, including the Platyrrhine monkeys, *Cercopithecus*, &c., I find no anterior communicating artery." In those lower forms, instead of the pair of large anterior cerebral arteries, there is but a single azygos-vessel, which in its course forward gives on either hand branches to the right and left hemispheres respectively. Apart from Mr. Parsons' morphological work, which has not yet appeared *in extenso*, the only description we know concerning the arterial supply of the brain in the anthropoid apes is furnished by Professor Bolk in his recent monograph on the naked eye features of the brain of the Orang. A detailed account is there given of the arrangement of the arteries at the base in two specimens of Orang brain. He writes[1]: "Die Hauptstämme werden auch hier durch die beiden Carotiden und Arteriæ vertebrales

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[1] L. BOLK. "Overdruk uit Petrus Camper Nederlandsche Bijdragen tot de Anat. I., i. II." "Ueber das Gehirn v. Orang-Utan."

dargestellt, welche intracraniell zwar anastomosiren jedoch bei keinem der zwei Exemplaren einen geschlossenen Circulus arteriosus bildeten, da die Arteria communicans anterior in beiden Fällen fehlte."

Our observations have been obtained on six Chimpanzees and on one Orang-outang. Of the specimens classed as Chimpanzees, one was of the variety termed the Koolakaamba, supposed by some observers to be a cross between *Troglodytes niger* and *Troglodytes gorilla*. The *Circulus arteriosus* found in five of these specimens was of what may be termed the human type. In three Chimpanzees, two large anterior cerebral arteries were united by a short junctional vessel, an *arteria communicans anterior*. In one Chimpanzee the junction between the two anterior cerebral arteries was not effected by a separate vessel coursing from one to the other, but by what amounted to a practical lateral fusion of the two trunks together in the middle line for a short distance, *i.e.*, about 4 millimeters. In the Koolakaamba the *circulus* was completed by a short but distinct *arteria communicans anterior*. So also in the Orang; our specimen possessed an anterior communicating artery, measuring *post mortem* 7 millimeters in length, and about 1·3 millimeters in diameter, and completing the *circulus* as it is completed in man.[1]

In a sixth specimen of Chimpanzee there was the single azygos anterior cerebral artery such as is found in the lower monkeys and in mammals generally.

A *Circulus arteriosus* of human type thus existing in these anthropoids, it becomes of interest to enquire as to the freedom in them of cross anastomosis in the blood supply of the cerebral hemispheres. This point we have examined in four Chimpanzees.

In none of these animals did occlusion of one common carotid produce either spasm or unmistakable alteration of the excitability to faradism of the motor region of the cerebral cortex. The blood-vessels for their occlusion were laid bare and silk ligatures passed under them. There is not the least doubt that on each occasion the vessel it was desired to occlude was closed absolutely throughout the whole of the desired period. The occlusion was maintained for eight minutes. In one case during the occlusion the pulsatile movement of the hemisphere where exposed, namely, over the fronto-parietal region, became imperceptible to inspection. But the motor responses to faradic stimulation tested each half minute revealed no obvious alteration.

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[1] The actual specimens were demonstrated at a meeting of the Liverpool Medical Institution, on February 20th, 1902.

In two Chimpanzees we found simultaneous occlusion of both carotids fail to evoke any convulsions or to extinguish or markedly diminish the excitability to faradism of the motor region of the cortex, although the complete double occlusion was maintained for eight minutes without any intermission. At the end of the second minute in one of these experiments the response of the leg area to faradisation seemed brisker than before the occlusion of the carotids, but this increase, whatever its origin, quickly subsided and the responses subsequently continued not noticeably different in any way from those obtained at the outset and before the occlusion. The leg-area in this experiment was the region examined by the stimulation, but in the whole of the exposed portion of the brain pulsation, as judged by inspection, was diminished even to extinction under the double carotid occlusion.

In a third Chimpanzee the similar experiment elicited results different to the above. Occlusion of both carotids suppressed the motor response of the cortex in 100 seconds in one hemisphere (right hemisphere) and in 120 seconds in the other hemisphere. The occlusion, it is noteworthy, did not produce convulsions. On releasing the carotids the excitability of the motor area to faradisation reappeared in 75 seconds in the left hemisphere and in about 85 seconds in the opposite.

In a fourth Chimpanzee, namely, that specimen found subsequently to have a *circulus arteriosus* of the ordinary mammalian type, and not resembling the human, occlusion of the right carotid alone produced no obvious alteration in the reply of the arm area of the right hemisphere during a period of five minutes of maintained occlusion. The

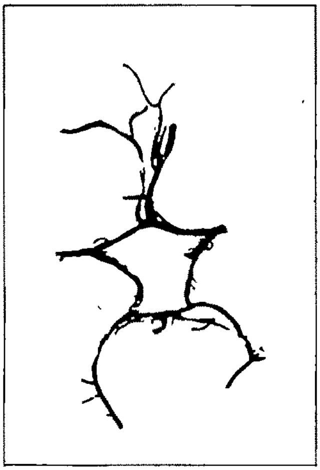

FIG. 1.

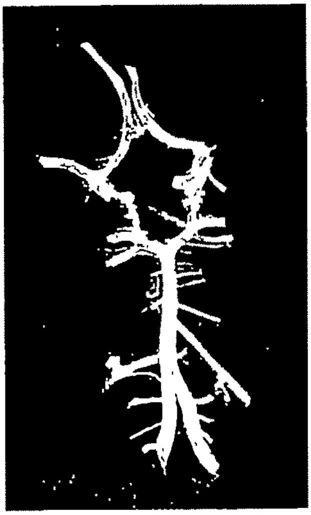

FIG. 2

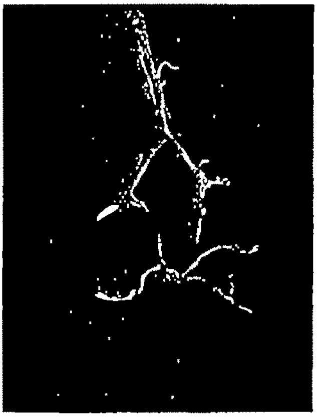

FIG. 3

Photographs of "Circles of Willis" from Anthropoid Apes.

FIG. 1.—From Chimpanzee.

FIG. 2.—From Orang-Utang.

FIG. 3.—From Chimpanzee, less usual type, the anterior cerebral arteries unite to a common trunk for a distance of four millimetres.

testing was made every half minute. Simultaneous occlusion of both carotids extinguished the reactions from the right hemisphere's arm area in four and a half minutes. The occlusion was maintained for a minute and a half after extinction of faradic excitability. Reactions became once more elicitable ninety seconds after the carotids had been freed.

The above observations establish, therefore, in the first place, that in the Chimpanzee and Orang an arterial circle of Willis of the human type is met with; although, as shown by Bolk's two Orang brains and by one of our Chimpanzees, it is not met with invariably. In the second place, they show that in collateral supply of the brain by anastomotic arterial provision, there is, just as with the morphology of the arterial circle, considerable range of individual variation. In some Chimpanzees the arterial anastomosis is found experimentally to have sufficient freedom for an occlusion of both carotids maintained for eight minutes, to make no obvious alteration in the faradic excitability of the cortex, at least, in its motor region. In other individuals such occlusion is found to rapidly paralyze the cortex, at any rate, in its motor region, when tested by electrical stimulation. This conclusion harmonises strikingly with the conclusion drawn by L. Hill regarding the efficiency of the circle of Willis in man. Hill states:[1] "The efficiency of the anastomosis through the circle of Willis varies in different individuals. Sudden compression of one common carotid artery in some men produces epileptic spasm, and ligation of this artery has been followed in some by more or less temporary paralysis on the opposite side of the body; in others the effect is *nil.*"

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[1] Schafer's "Textbook of Physiology," vol. ii., p. 148

EXPERIMENTS ON THE CONDUCTIVITY OF THE SPINAL CORD RENDERED ANÆMIC BY COMPRESSION OF THE AORTA.

BY MAX LOEWENTHAL, M.D.WÜRZBG., M.R.C.P.LOND.

HISTORICAL RECORD.

SINCE Nicolas Steno stated in 1667 that occlusion of the aorta is followed by paraplegia, this subject has received the attention of many investigators. This phenomenon, also observed by Haller and Sir Astley Cooper, was considered to be of peripheral origin, until, nearly two centuries after its discovery, Kussmaul and Tenner showed that the "paraplégie ischémique," as it was later named by Jaccoud, is not due to anæmia of muscles and nerves, but to anæmia of the spinal cord. A year afterwards, Sir William Gull published his clinical observation of a case of paraplegia following obstruction of the abdominal aorta within two minutes. Schiffer and Weil and other writers corroborated Kussmaul and Tenner's views. At about the same time Richet and Claude Bernard studied the effect arrest of the circulation has on the reflexes.

The former observed that in the rabbit the reflexes are arrested in less than one minute, the latter, and after him Freusberg, that they persist much longer in mammals, if the animal has previously been cooled for some hours, or if the circulation has been artificially weakened. According to Bernard, the warm-blooded animal loses its spinal excitability quicker than the cold-blooded, the bird quicker than the mammal.

Schiff made a very interesting observation. If the spinal cord of a cat has been severed in the thoracic region and the circulation arrested in the isolated portion of the cord, powerful contractions of the muscles of the hind limbs and tail ensue. He as well as Richet observed that a high degree of anæmia does not at once abolish, but rather increases, the sensitiveness of the nervous system, and bled dogs in order to heighten their reflex excitability. Richet is the first to make the following important remark with regard to the human subject :—"Abundant hæmorrhages augment the medullary excitability. The greater excitability of the nervous system in chlorotic (patients) coincides with the general anæmia." This appears to be a general law in the animal tissue, for Richet found this initial increase of activity in anæmia also in the peripheral nerves, and instances the painful attacks of Raynaud's disease and the sometimes severe pain following ligation of arteries. The same holds good, according to Faivre, for the nerves and muscles of the frog. Richet also compressed the bulb of the aorta in the rabbit, and found the eye reflex gone after four seconds. If the circulation was interrupted for forty seconds, its re-establishment failed to restore muscular movements and reflexes.

The effects of ischæmia were slower to come in young than in old animals. The above statements as regards an initial increase of activity of the anæmic cord, are supported by Prévost's researches, who, after compression of the abdominal aorta, observed first exaltation and afterwards depression of the knee-jerk. Important contributions to the subject of spinal anæmia were also made by Fredéricq, Colson, Münzer and Wiener, and Brown-Séquard.

The following contributions are of a more recent date. H. E. Hering tried to solve the question, whether it is only the highly vascular gray matter that is responsible for ischæmic paralysis, or whether the white matter has a share in it. He found that simultaneous compression of the carotid and vertebral arteries render the cerebral white matter inexcitable or incapable of conduction, so that cerebral stimulation failed after a certain time to penetrate into the medulla and to evoke the muscular response. From this he concludes that compression of the aorta will likewise deprive the white matter of the cord, especially its long tracts, of their conductivity, there being no essential difference between the cerebral and medullary white matter, neither as regards their structure nor their vascularity. Unfortunately the article does not give the length of time which elapses from the moment the blood supply has been cut off until the conductivity is destroyed. As long ago as 1881, Minkovski (cited by Hering) made the same experiment, and obtained the same results.

The well-known degeneration succeeding a prolonged compression of the aorta exhibits some peculiarities which, in contrast to Hering's deductions, show a great resistance of the white matter against prolonged anæmia; for, according to Ehrlich and Brieger, Colson, and other writers, there is hardly any degeneration to be found in the posterior roots, dorsal columns, and pyramidal tracts, but especially in those fibres which originate in the central gray matter. The degeneration in these fibres is not a primary one, but a secondary degeneration caused by destruction of the mother cell. The intervertebral ganglion is not easily destroyed, and cannot be considered functionally equivalent to the gray matter. All those fibres which hail from undamaged cells escape, although they have also been exposed to a prolonged lack of nutrition. If these long tracts are not destroyed by an hour's compression of the aorta, it would be very remarkable indeed if the white cerebral substance lost its conductivity in a few minutes. I shall return to this question later. Langendorff has proved by experiment that ischæmic anæsthesia does not originate in the intervertebral ganglion, but in the posterior cornua. Another proof has been given by H. E. Hering, who compressed the aorta in rabbits and found that stimulation of the central stump of the posterior root evokes no reflex movements, nor did he obtain any reflex by dipping the animal's paw into hot water. This shows that the primary interruption of the reflex path must be situated inside the medulla.

Ascher and Arnold performed a series of experiments on the same subject, and found that the different functions of the spinal cord are not destroyed simultaneously, but in a certain succession. Motility is lost first, whilst the sensory paths still conduct, for at a time when the posterior half of the rabbit is already motionless, stimulation of the crural nerve excites movements of the anterior extremities. After this distant reflex is abolished, there remains as the last visible reflex a slight alteration in the breathing. The very last surviving reflex is a distinct rise of the blood pressure.

When studying the experimental anæmia of the spinal cord, one must strictly distinguish between its excitability and its conductivity for impulses coming from outside the cord. The conductivity may be altered for centripetal and centrifugal impulses. The former, as the historical record shows, has been the subject of much research, but the latter has hitherto, to my knowledge, received no attention.

At the suggestion of Professor Sherrington, I commenced a series of experiments in February, 1899, in order to study the effect which complete anæmia of the spinal cord has on its conductivity for centrifugal impulses, and, besides, repeated some of the experiments performed by others with regard to reflexes.

METHOD OF EXPERIMENTING.

The animals experimented upon were cats. Employing the usual method first, I rendered the lower end of the spinal cord anæmic by compressing the abdominal aorta, but soon abandoned this method, as I found that digital compression of the thoracic aorta can be done more exactly and easily, and moreover excludes a larger portion of the spinal cord from the circulation. A convenient way of compressing the thoracic aorta, is to introduce the index finger, after resecting part of the sixth or seventh rib on the left side, into the pleural cavity, and to compress the aorta against the vertebral column between the index finger and the thumb of the same hand placed outside.

As deficient aëration of the blood owing to collapse of one lung might mar the value of the results, I deemed it advisable to keep up artificial respiration. For this purpose tracheotomy was performed, and the stem of a T-shaped glass cannula tied into the trachea. One of the cross branches of the cannula was partly closed with wax to regulate the amount of air passing through the lungs, whilst the second branch was connected by rubber tubing with an automatic air pump worked by a dynamo. In the course of this rubber tube, I inserted a Wolff's bottle for the administration of an anæsthetic, which was either an ether-chloroform mixture or pure ether.

I first endeavoured to determine the length of time during which the spinal cord retains its conductivity for a stimulus arising from the cerebral cortex, from the moment the blood supply is cut off. To this end, the left motor area of the brain was laid bare by removing the piece of skull covering the left crucial sulcus with trephine and bone forceps and carefully opening the dura mater.

EXPERIMENTAL OBSERVATIONS.

(A) *Cortical Stimulation.*

In the first animal experimented upon, a fit commencing in the posterior extremities, was produced on stimulating the hind limb area of the cortex by a faradic current just strong enough to give a response. The aorta was then compressed for two minutes, and the current applied to the same area again. The hind limbs gave no response now, their muscles being atonic and flabby, whilst the fore limbs showed the usual clonic movements.

In the second experiment, the aorta was again compressed, and after two minutes the cortex stimulated, when the fore limbs responded vigorously, and the hind limbs remained motionless and flaccid. On releasing the aorta, the right hind limb was suddenly and spontaneously drawn up for a few seconds. After an interval of ten minutes, the aorta was compressed at the same moment in which excitation of the cortex was commenced, the latter being stimulated for a few seconds at intervals of about ten seconds. At first the hind limbs responded distinctly more vigorously and promptly than before compression, and with quickly increasing strength, until after about forty seconds the movements began to be weaker, and finally ceased after about sixty seconds. The preponderance of the movements of the hind limbs at the commencement and of those of the fore limbs towards the end of this minute was very distinct. On releasing the aorta after a minute's compression, both hind limbs were immediately drawn up, but this flexor spasm only lasted a moment. This phenomenon I could often observe, if the compression had not lasted much longer than a minute. Repetitions of this experiment in the same animal gave similar results with the difference that the hind limbs became paralysed sooner at every following trial. Similiar results were also obtained in several experiments performed on other animals under the same conditions. After a time averaging eighty seconds, the hind limbs remained motionless. I could always notice an increase in the strength and readiness of the response during the first half, and a decrease, especially quick towards the end, in the second half of the time, during which movements could be obtained. The time which elapses before a response can again be obtained in the hind limbs after re-establishing the circulation, greatly depends on the length of time during which the circulation was interrupted. After two or three minutes the cord has regained its conductivity, unless the anæmia has lasted too long.

(*B*) *Spinal Fits.*

Three or four times, I could observe a peculiar phenomenon in different animals. At the time when ischæmic paralysis was commencing, the hair of the tail became erect and immediately afterwards a powerful extension tonus with slow writhing movements of small range seized the posterior half of the animal's body. There was flexion of spine and hips and extension of tail, knees, and ankles. I was struck with the likeness between these localised convulsions and those agonal general convulsions one observes in animals bled to death or asphyxiated, and am therefore tempted to describe these movements as localized or partial agonal convulsions. The contractions of muscles observed by Schiff after section of the cord are probably identical with those observed by myself. Section of the cord may facilitate the occurrence of this phenomenon, but is not essential. These convulsions could several times be brought on by stroking the tail after conduction from the cerebral cortex was abolished. They certainly originate in the gray matter of the spinal cord and therefore deserve the name of "Spinal Fits." Probably the whole of the motor portion of the gray nervous matter is capable of violent explosive discharges, and every accumulation of motor cells throughout the brain and medulla can act as a "cramp-centre." Cortical discharges are of the well-known clonic type and those of the spinal cord chiefly tonic, whilst discharges of the bulbopontine gray matter (Kussmaul and Tenner's "cramp-centre") are a mixture of tonic and irregularly clonic, jerky movements. Thus Hughlings Jackson's different levels are represented by different kinds of discharges.

(*C*) *Knee-jerks.*

Four experiments were made in order to study the knee-jerks after compression of the aorta, and it was found that they present the same peculiarity as the cortical response. Instead of gradually becoming weaker from the commencement, the knee-jerk on the contrary shows a rapid increase, until after about half a minute the slightest tap, almost a touch, on the patellar tendon elicits a vigorous jerk. It then gradually lessens and quickly subsides altogether after about eighty seconds. Its re-appearance takes about the same time as that of the cortical response from the time the circulation has been restored.

(*D*) *Peripheral nerves and posterior roots.*

When stimulating the sciatic nerve after compression of the aorta, I could get no reflex movements after from two to three minutes. These movements not being so obvious as the knee-jerk in an anæsthetised animal, it is difficult to state the exact moment when they have ceased, but they last distinctly longer than the knee-jerk. I could not make out an initial increase such as I observed in the knee-jerk and on cerebral stimulation. Dipping the animal's hind paw into hot water, I could twice observe movements of the fore limbs and forced breathing at a time when the hind limbs were completely motionless. Stimulation of the posterior roots is apt to lead to fallacies, as it is very difficult to be certain that the current is not straying into the cord. On applying a very weak current to the posterior roots at the lumbar enlargement, movements were obtained if the electrodes came too near the cord, but no movement could be elicited at a greater distance unless the strength of current was increased. The same weak current which just gave the response before compression of the aorta, failed to do so after two minutes compression. I was struck with the great irritability of the anæmic spinal cord, and with the length of time it lasted. It even seemed to me that for a long time it is even more irritable than normally. The weakest current applied as late as fifteen minutes after death at the insertion of the posterior roots gave a violent response. Personal observation leaves me no doubt that this is a real reflex carried from the points of entrance of the sensory roots to the motor cells and that it is not due to the anterior roots being stimulated by stray loops of current. If the ventral aspect of the cord is stimulated, the muscles of the same side contract steadily, but if the current affects the vicinity of the posterior roots, the muscles respond also on the other side, and in a jerky manner, giving a series of contractions quickly following each other and greatly resembling the pain reflex.

REMARKS.

The first conclusion that can safely be drawn from my own and from other experimenters' results, is the fact that after about two minutes of complete ischæmia no stimuli entering the ischæmic part of the medulla can penetrate into the motor nerve. My experiments prove that stimuli coming from the cerebral cortex do not form an exception to this rule. The question which remains to be solved concerns the nature and the place of this obstruction to the flow of the nerve current. If Hering's view is correct, the white substance loses its conducting power as well as the gray, and no energy can enter the anæmic part of the cord. It is, however, extremely unlikely that the fibres of the white columns should be deprived of their conductivity in so short a time, as I have already pointed out before. There are several facts opposed to this view. The peripheral nerves, retaining their conductivity for a very long time, resemble the fibres of the central nervous system, from which they only or chiefly differ in their possession of Schwann's sheath, anatomically and functionally, and we should therefore expect a similar power of resistance to a lack of nutrition in both. We know that in prolonged anæmia those fibres which are derived from undamaged cells escape degeneration, though they have been without their blood supply as long as an hour. Why, then, should we believe that they lose their conducting power within a few minutes?

The vascularisation of the white cerebral and medullary substance, moreover, is so scanty that it cannot be greatly dependent on a liberal supply of blood, but it seems to me, apart from these considerations, that Hering's and Minkovski's experiment, however interesting it may be, is not conclusive. It certainly proves that compression of the arteries supplying the brain prevents a stimulus arising from the corona radiata from reaching the motor cells of the anterior horn, but it does not prove that the white substance, in our case the portion of the pyramidal tract coursing through the anæmic area, has been deprived of its conductivity. The main motor path in the lower animals cannot go through the pyramids, for their section in front of the medulla oblongata does not appreciably affect the animal's movements. This being so, it must be proved first that their stimulation under proper precautions can evoke muscular action in the lower animals. The main motor path traverses a complex mechanism containing gray matter, and would, on account of the latter, be interrupted by compression of the cerebral arteries. Another point to be considered is the depression, or even suppression, first observed by Landois, of cardiac action and respiration caused by ligaturing all the cerebral arteries. This in its turn may depress the activity of the medullary gray matter and act similarly to compression of the aorta. It is my opinion that we must seek the place of interruption in the gray matter, at the points of transit from one neuron to the other.

We do not know how long after anæmia is established the gray matter remains excitable. The fact that stimulation by a very weak current of the tip of the posterior horn excites bilateral muscular movements, may be due to "Stromschleifen." According to Schafer's "Text-Book of Anatomy," some of the fibres of the anterior roots take their origin in cells of the posterior horn; others go from the anterior horn through the white commissure and leave the cord in the motor roots of the opposite side. This commissure being in the lumbar region situated in the centre of the cord, it is possible for loops of the current straying from the electrodes to reach it, thereby causing bilateral movements. The resulting muscular response, however, resembles that of the pain reflex very closely, and gives one the impression that the stimulus is conducted by the gray substance of the posterior horn to the motor cells. This reaction begins to fade after the lapse of about fifteen minutes.

The remarkable experiments performed by Hoche on the human subject add weight to the latter view. He obtained permission to study the functions of the spinal cord in several decapitated criminals immediately after the execution, and managed to commence his experiments as early as two minutes after the head was severed from the body. He found that no movements of the legs could be obtained by applying the electrodes to the pyramidal tracts exposed in the cut surface, nor could the patellar reflex be obtained. Stimulation of the ventral half of the cord with a minimal current and electrodes 1 mm. apart gave movements in the shoulder and elbow joints of the same side, whilst stimulation of the posterior root was followed by bilateral, exactly symmetrical movements of a different character, crossing of the arms before the chest. Although it is possible that Hoché employed too strong a current, and, consequently, stimulated not only the posterior roots, but also the adjoining parts of the cord, his experiments render the existence of an intimate connection between the sensory and motor gray matter, not quickly severed by death, highly probable.

CONCLUSIONS.

(1) The first effect of arrest of the circulation on the functions of the spinal cord is an increase in the readiness and strength of interneural transmission of nerve energy lasting about thirty seconds.

(2) After from one to two minutes, stimuli approaching the gray matter through peripheral nerves or the fibres of the white substance, are not transmitted to the lower motor neuron.

(3) It is probable that every single neuron as a functional unit retains its vitality for a period exceeding fifteen minutes, but that the mechanism which links the separate neurons together is quickly destroyed by death.

(4) The existence of genuine spinal fits cannot be disputed.

The experiments described in this paper were performed in the Physiological Department of the Thompson-Yates Laboratories. My sincerest thanks are due to Professor Sherrington for much valuable advice and help, and to Dr. Hope-Simpson, who devoted much of his time to this research, for his able assistance.

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FURTHER OBSERVATIONS ON A CASE OF CONVULSIONS (TRUNK FIT OR LOWEST LEVEL FIT ?).

BY J. HUGHLINGS JACKSON, M.D., F.R.S.

AND

STANLEY BARNES, M.D., M.R.C.P.

PART I.[1]

THIS is a further report of a case published (BRAIN, Spring No., 1902, part 97), by Dr. Douglas Singer and myself. Although it is convenient, following custom, to use the term *status epilepticus*, the important question, as we then said, is not whether the fits the patients had are to be called epileptic or not. The really important question is, to reproduce part of what we wrote (*op. cit.*), "Where is the lesion (discharge-lesion) which, on its occasional 'intense' discharge, produces a convulsion *beginning* in muscles of the trunk (that is, in muscles of two sides of the body, the normal action of which may be, and often is, bilateral) and *beginning* in those muscles of the two sides of the body simultaneously?" It will be seen that in the "first period" of the *status* Dr. Stanley Barnes describes, the convulsion did not affect the extremities in the slightest degree. In the "second period" the limbs were affected, but after the trunk; Dr. Barnes carefully describes a "march" of the spasm *down* the arms. As ought always to be done, he distinguishes between movements proper, in two attacks of the first period, and spasm (contention of many movements). I think now, considering especially the observations Dr. Stanley Barnes made on the "inspiratory cry" in a certain part of the march of some of the patient's attacks, that her fits are probably Lowest Level (Ponto-Bulbar) Fits and not fits of ordinary Epilepsy (Higher Level Fits).

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[1] The first part is by J. H. J., the second by S. B.

I draw particular attention to Dr. Barnes' observations on the reflexes in and after the fits; these observations seem to me worthy of great attention. It is very striking that the knee-jerks were lost *in* attacks when there was not the least spasm of any limb.

PART II.

History.

The patient, J.K., is the eldest of a family of nine children, all of whom are alive. Most of the other children are said to have a "narrow bridge" to the nose, but no history of any other sign of syphilitic taint can be obtained.

The patient has always had a squint, and in childhood suffered from measles, whooping cough, and scarlet fever. For about two years during the first dentition she suffered from "teething convulsions."

The present illness began at the age of 9 years; the fits at first occured about once a month and gradually increased in frequency. After the age of puberty, their number rapidly increased to several daily. In March, 1901, she was in *status epilepticus* for ten days, followed by a period of complete cessation for a month; the fits then recurred, and in December, 1901, she again passed into *status epilepticus* for sixteen days. At this time she was admitted to the National Hospital, and many of the fits were observed (*vide* BRAIN, Spring, 1902, "Observations of a case of Convulsions" by Dr. Hughlings Jackson and Dr. Douglas Singer). She remained in hospital for three months longer, and during this time only had one slight attack. The patient then went to the Convalescent Home at Finchley, where she remained for nearly two months, a few slight seizures occurring there. During the second week after her return to her own home a few severe attacks came on, and these continued to occur and increase in number until the fifth week, when for the third time she passed into *status epilepticus*, and was re-admitted to the National Hospital on June 13, 1902.

General Examination.

As in the previous attack of *status epilepticus*, the general examination was deferred until consciousness was regained on

June 27. No material change in her general condition had occurred since her previous admission in December, 1901, so that it is unnecessary to repeat here the description given in the previous paper (*vide* BRAIN, Spring, 1902, p. 125).

The Fits.

The first ten days after admission some 200 fits a day were seen to occur; it is highly probable that the actual number was even larger. The maximum recorded was on the second day, when 394 were observed. After the tenth day the number rapidly diminished, and on the fifteenth day no fit occured. From that day (June 27) until September 2 only one severe and three slight attacks occurred at irregular intervals.

In describing the attacks it will be convenient to classify them as in the previous paper, according as they occurred in the earlier or the later stages of the *status epilepticus*.

Fits occurring in the First Period.

The attacks occurred at intervals of about three minutes, each attack lasting about forty seconds. She was unconscious between the attacks.

Before the attacks, the patient was lying on her back in bed with her head resting on a pillow, the arms lying, as a rule, in front of her. The breathing was quiet and regular, both chest and abdomen moving about normally for a girl of her age; the accessory muscles of respiration were not in action during inspiration.

In every instance in which the onset was particularly watched, a bilateral deepening of respiration with action of the sternomastoids and scaleni was the first sign of an approaching fit. These accessory muscles of respiration did not at once go off into tonic spasm, but contracted in inspiration and relaxed in expiration; after two such inspirations, in the second of which the contraction was more marked than in the first, the sternomastoids and scaleni failed to relax completely in expiration, so that the chest remained unusually expanded although respiration continued for several seconds afterwards.

The contraction of the accessory muscles of respiration appeared to be equal on both sides; it was not very powerful, and the head was never lifted off the pillow; at times a slight rotation of the head occurred, sometimes to the left, occasionally to the right.

Usually at the end of the second inspiration mentioned above, the next movement occurred; this was a contraction of the frontales and levatores palpebrarum of both sides symmetrically. The eyes then turned jerkily to the left, the elevators of the eyebrows and eyelids being at this time in tonic spasm.

The lower segment of the face was next affected, both sides at the same time, but, as a rule, the left side slightly more than the right; the angles of the mouth were drawn downwards and the lips separated. Tonic spasm here rapidly gave way to clonic spasm, but before the latter was fully established the jaws were separated by a tonic spasm of the depressors of the mandible overcoming the contracting masseters and temporals. The teeth, as a rule, were separated about half an inch, and the jaw always opened strictly in the middle line.

Up to this point respiration had continued at the usual rate, although the scaleni and sternomastoids were contracted apparently as much in expiration as in inspiration. Just as the jaw opened, the chest being full, respiration ceased, but not all respiratory movement. The abdomen swelled slowly forwards (diaphragmatic action), and at the same time the chest slowly sank in and diminished in volume, no air either entering or emerging from the glottis. This complex movement continued for about twelve seconds, and then ensued a long-drawn crescendo inspiratory cry; at the beginning of this cry the pitch was high, and gave the impression of air entering the chest through a very narrow glottis owing to great inspiratory effort; later the spasm of the glottis appeared to give way and allow air to enter more and more freely. The cry lasted about five seconds, and as it occurred the abdomen remained fixed in its inspiratory position whilst the chest again filled out. After the cry the respiration was resumed almost at once, and, as usual in her sex, was of the costal type. The eyes before the cry were turned to the left; after it, as they slowly returned to their usual position, the conjunctivæ became suffused and much lachrymation occurred, the tears usually rolling down both cheeks just at the end of the fit.

In the majority of the fits very little cyanosis occurred; in one that was carefully observed there was very marked blueness just before the cry. No noticeable sweating occurred.

In none of the fits did the slightest spasmodic hand or arm movement occur. In two of them, just as the fit was beginning, an irregular purposive-seeming movement was going on in the right upper extremity, the elbow being flexed and the forearm pronated as though she were going to rub her eyes—a thing she often does between the attacks. There was no spasm about the movement, and it was of an absolutely different nature from the face and neck movement; it never occurred whilst the fit was in progress after the corneal reflex was lost. Apart from this movement, not a trace of muscular contraction occurred in the upper extremities, which were loose and slack at all their joints. The lower extremities were also carefully observed repeatedly, but no movement or muscle contraction could be felt here.

During the attacks the patient was quite unconscious, and she often micturated in or after them. The reflexes were carefully observed in many of the attacks, and deserve mention in some detail.

State of Reflexes in the Fits.

The *corneal reflexes* were only lost at the height of the fit; they began to diminish as soon as the elevation of the eyebrows occurred, and were lost at the time when the jaws were separated. They returned before the face had ceased to twitch, and quickly reached their normal intensity.

The *supra-orbital* reflexes disappeared during the attacks, during, speaking roughly, the same period as the corneal reflexes.

The *jaw-jerk* between the attacks was unusually brisk; it remained so during the attacks, except when the jaw was fixed by spasm of the mandibular muscles.

The *knee-jerks* were carefully and repeatedly tested during several attacks. The method adopted was to support the thigh so that the leg hung down at an angle of about 120°, and the ligamentum patellæ was then tapped with a percussion hammer about once a second, beginning before the commencement of the fit and ending after the end of the fit. Each knee-jerk was tested in several fits. Between the attacks the knee-jerks were brisk, and no alteration occurred at the beginning of a fit until the lower part of the face went into spasm, and breathing had ceased; at this stage the knee-jerk rather suddenly completely disappeared, and remained absent until the cry occurred; it now at once began to return, and just at the end of the fit was more brisk than usual, resuming its usual slightly brisk condition a few seconds later. This observation was confirmed by Dr. Hughlings Jackson and by Dr. Risien Russell on separate occasions. At the risk of appearing tautological, I would reiterate that in these attacks in which the knee-jerks were lost not the least movement or spasm of any limb occurred.

Fits of the Second Period.

On June 22, for the first time, fits were observed in which limb movements occurred. On this day these fits to a large extent alternated with those previously described as "fits of the first period," and in which no limb movement occurred. It was noticeable that the fits in which limb movement occurred were of longer duration and apparently of greater severity than those in which no such limb spasm was present. Repeated and careful observation convinced me that the fits of the two periods began in exactly the same way, the difference being that during the second period, in many instances, the fit spread from the trunk to the limb muscles, so that in the most severe attacks the spasm became general.

The first limb movement to occur was always at the proximal end of one of the upper extremities; usually the left, sometimes the right shoulder group was first affected, the point of the shoulders being shrugged upwards, the arm elevated forwards, then the elbow was flexed, the wrist extended, and the fingers were strongly flexed over the thumb, which was adducted into the palm; in this way the fit could be observed to spread from the proximal to the peripheral terminal muscle groups. The movements were at first tonic and afterwards clonic.

In the lower extremities the extensors of the knee appeared to be first affected; beyond this I was unable to trace the order of involvement of muscle groups, as only two fits were observed in which the legs went into spasm. When in full spasm, however, the legs were, in these two attacks, in the fully extended position, *i.e.*, with extension at hip, knee and ankle. The first lower extremity movement appeared to begin a little later than the first upper extremity movement, but before the whole upper limb was involved. I cannot say whether the left or right leg was the more frequently affected.

None of the above-described limb movements ever occurred until after the "cry" (*vide* "Fits of the First Period").

Slighter Fits.

Beyond the two kinds of fits already described, many slighter attacks were frequently occurring during both periods. In their onset these fits exactly resembled those described as "fits of the first period," but instead of going on until the jaw was depressed, they died away as soon as the upper part of the face had become involved; there was no cry with these attacks. Every gradation was observed between these slighter attacks and the more severe ones in which the limbs were fully involved.

Mental Condition.

Until June 27, the day on which the fits ceased, no reply in answer to a question could be got from the patient; nor did she utter any sound which would lead one to suppose that she was at all conscious. On that day she first began to speak, but it was evident that she was only dimly conscious, and her ideas appeared to be much distorted. At times also she appeared to be suffering from hallucinations of vision and hearing. By June 28 she could reply sensibly to very simple questions, and thereafter she gradually resumed her usual mental state, so that by July 18 she could write letters passably well.

Incontinence of urine and fæces continued for nearly a week after all fits had ceased, but is now (September 8) no longer troublesome.

HEREDITARY APHASIA: A FAMILY DISEASE OF THE CENTRAL NERVOUS SYSTEM, DUE POSSIBLY TO CONGENITAL SYPHILIS.

BY WILLIAM GREAM STONE, M.A., M.D.OXON., F.R.C.S.

AND

JOHN J. DOUGLAS, M.D., F.R.C.P.EDIN.

I.

UNDER the title of Hereditary Aphasia we have attempted to describe a disease that has been observed in eight members of a family; three cases occurring in one generation, and five in the generation following. There is a sufficiently close resemblance between each one of the series of cases and the rest to exclude the notion of an accidental similarity, and to justify the conclusion that we have to deal with one disease in all the cases, a disease due to the same cause throughout, and capable of recognition if it recurs by a limited group of well defined symptoms. The morbid anatomy and histology have been worked out in the latest of the cases, and the lesions observed suggest, though far from conclusively, a syphilitic origin for the disease. If this point can be proved, it will be of special interest, for the taint of the disease will have reached the grandchildren of the person originally affected.

The main features of the disease, which does not become manifest until the patient is attaining to adult life, are the following:—Incontinence of urine,[1] attacks of temporary aphasia with loss of power on the right side of the body, gradually increasing opacities in the vitreous humor of the eyes, loss or diminution of the senses by which pain and temperature are appreciated, muscular weakness, epileptiform convulsions, and sudden death preceded by complete unconsciousness. Wasting of the soft tissues is marked only during the later stages of the disease.

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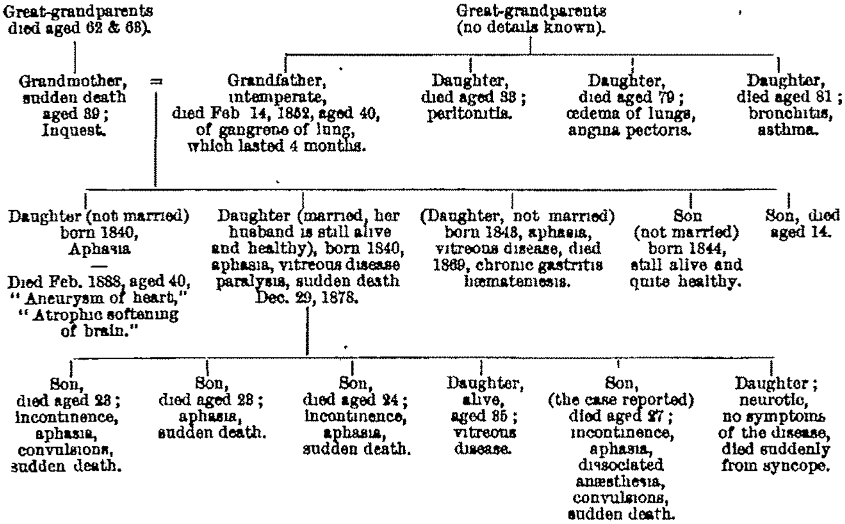
[1] The term incontinence is here used, as the affection was so described in the earlier cases; but the symptom would be more correctly described as "retention of urine."

A family tree will briefly show the number of children in each generation, and how they were affected by the disease:—


Great-grandparents died aged 62 & 68).
Great-grandparents (no details known).
Grandmother, sudden death aged 89; Inquest.
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Grandfather, intemperate, died Feb 14, 1852, aged 40, of gangrene of lung, which lasted 4 months.
Daughter, died aged 38; peritonitis.
Daughter, died aged 79; œdema of lungs, angina pectoris.
Daughter, died aged 81; bronchitis, asthma.
Daughter (not married) born 1840, Aphasia — Died Feb. 1888, aged 40, "Aneurysm of heart," "Atrophic softening of brain."
Daughter (married, her husband is still alive and healthy), born 1840, aphasia, vitreous disease paralysis, sudden death Dec. 29, 1878.
(Daughter, not married) born 1848, aphasia, vitreous disease, died 1869, chronic gastritis hæmatemesis.
Son (not married) born 1844, still alive and quite healthy.
Son, died aged 14.
Son, died aged 23; incontinence, aphasia, convulsions, sudden death.
Son, died aged 28; aphasia, sudden death.
Son, died aged 24; incontinence, aphasia, sudden death.
Daughter, alive, aged 35; vitreous disease.
Son, (the case reported) died aged 27; incontinence, aphasia, dissociated anæsthesia, convulsions, sudden death.
Daughter; neurotic, no symptoms of the disease, died suddenly from syncope.

It will be seen from this that there is no evidence of the disease in the great-grandparents on either side. Of the maternal grandparents, both furnish some suspicious points. The grandmother died suddenly, so suddenly as to require an inquest. The coroner's verdict, however, gives no details, only stating that "she died naturally and not from any "violence." The grandfather led an intemperate life, and died in the London Hospital when 40 years old of "gangrene of the lung." This was a chronic illness, lasting four months, but unfortunately no *post-mortem* examination was made, and no record of the case has been preserved to show whether the disease was syphilitic or not.

Of the second generation one male is now alive, and healthy, at the age of 67. He was younger than his three sisters. The only other male child died in his fifteenth year, presumably too early to show symptoms of the disease. The three daughters all suffered from it. The mother of our patient was healthy as a girl and while a young woman. The only abnormal fact that is related of her previous to her marriage is that she suffered from time to time from a "curious reddish eruption on the finger-tips." She was married at 27, and shortly afterwards began to suffer from attacks of aphasia, which came on at long intervals, "perhaps two or three times in the year." On these occasions she also "used to drop things." Seven years after her marriage, at the age of 34, her sight had become so much affected that she only retained a weak perception of light. Whether she suffered from urinary troubles cannot now be ascertained. She died at the age of 38, after four years' partial paralysis, the latter appearing to have taken the place of the occasional attacks at about the same time that the amblyopia became extreme. Her death occurred on December 29, 1878, and was ascribed to apoplexy.

Of her two sisters, the elder died on February 6, 1880, aged 40. Death was ascribed to an "aneurism of the heart," supervening upon "atrophic softening of the brain"; the latter had been of several years' duration. It is remembered of her that she had temporary attacks of aphasia, with loss of power in the right arm. She had no epileptiform attack, or at all events, none that caused unconsciousness. She does not seem to have suffered from any ocular trouble, and there is no evidence of "incontinence of urine."

The younger sister died July 14, 1869, aged 26. Her death was due to hæmorrhage from a gastric ulcer. She suffered from temporary attacks of aphasia and paralysis in the right arm; and also, like her married sister, from a gradual loss of vision. The following account of the eye symptoms in both of his patients has kindly been furnished to us by Mr. Brudenell Carter, whom they consulted twenty-seven years ago; it is especially interesting in conjunction with Mr. Lawford's report on our patient, which is given later. "(The married sister) had slight deep-seated cloudiness of the vitreous, when seen in 1875, with slight impairment of vision; the right eye to about a $\frac{1}{3}$, the left to about $\frac{2}{3}$ of normal vision. Partly from the nature of the case and partly from the treatment by hyd. perchlor. and pot. iod., I have little doubt that I regarded the case as specific, but my notes do not say so. My last record is that the vision remained stationary, after slight improvement." This note was made three years before the patient's death, and, as has already been mentioned, blindness became almost complete before the end. Of the other sister Mr. Brudenell Carter writes: "I saw her on December 10, 1874, and on January 3, February 1, and March 23, 1875. My first note is, "Turbidity of R. vitreous, commencing ditto in L., probably hæmorrhagic in origin. Neurotic tendencies; occasional speechlessness with temporary paralysis of right arm. Under treatment the vision of R. rose from $\frac{8}{50}$ to $\frac{8}{25}$; the urine was normal."

We now come to the generation of the patient with whose case the present writers have been acquainted. There were six children, four sons and two daughters. The three elder sons died between the ages of 22 and 24. Of the two daughters one was older, one younger, than our patient. The elder of the two was healthy till her 30th year, but since then her eyesight has become defective, and the nature of the defect proves in this case also to consist in vitreous opacities. She is not known to have had any other symptoms of the disease. The younger daughter was neurotic, but showed none of the special symptoms characteristic of the disease. She died suddenly at the age of 24, from sudden heart failure during a severe attack of diarrhœa. There was no *post-mortem* examination.

The eldest son died at the age of 23, death being ascribed to "apoplexy." The first symptom of disease in his case is said to have been incontinence[1] of urine, which commenced in his twenty-second year. Previous to that time he had enjoyed good health, being educated at a public school where he played cricket and other games. After leaving school he

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[1] Probably really retention.

"crammed" hard for the army. The "incontinence," at first intermittent, gradually became established; it was presently followed by attacks of aphasia, short in duration. Later on he had several epileptiform seizures, falling in the street and elsewhere; he never hurt himself seriously by these falls, but he became quite unconscious, and the tongue was bitten. He was not drowsy after the attacks. It is also reported that he occasionally became unconscious for a few minutes without other symptoms.

The second son was healthy as a boy, but did not go in for any form of athletics. He reached the age of 22 without misadventure; but then, one morning at breakfast, he suddenly lost the use of his right hand, while trying to lift the cover off a dish. The weakness lasted for two or three hours. There is some doubt as to whether aphasia was also observed at this time; but later on he did have one or two attacks of aphasia, and it was decided to send him for a long voyage to Australia on account of his "want of tone." He improved during the early part of the voyage; but one day, in rough weather, he was found insensible in his cabin, and he died without recovering consciousness. He does not seem to have suffered at any time from urinary troubles.

The third brother was also healthy for the first 22 years of his life. He played cricket and football at school, and went into his father's office when he grew up. He died at the age of 24, having been ill two years. He had suffered from "incontinence" for about twelve months before his death. He also suffered from attacks of temporary aphasia, and those who were with him related that the lips became full and the face congested before an attack. He suffered greatly from constipation, sometimes passing no motion for a week; he gradually grew weaker, heavier, and more drowsy; finally he became suddenly unconscious, and died. Towards the end, when very weak, he passed fæces as well as urine unconsciously.

The fourth son was the only one known to us, who saw him first in December, 1897. He was then 23 years of age, and had begun to show symptoms of the disease about nine months previously. His appearance was that of a strongly built, rather tall young man. He had been healthy during boyhood and fond of all forms of athletics, including gymnastics, cricket and football. He had not suffered from incontinence as a child. There is no record of illnesses in childhood, except some unnamed illness at about the age of 14, a bilious attack followed by fever and delirium. At times he had been given to sleep-walking. As recently as 1895, when 20 or 21 years of age, he had been able to walk thirty-two miles in a day without more than ordinary fatigue.

In his case also the earliest symptom observed had been "incontinence of urine"; though an unusual degree of constipation had been present for two years before this occurred. It was preceded by pain in the tip of the penis, sufficiently severe to make him consult a doctor: the first escape of urine followed a week later. Since that time it had occurred only during the night; but, with three exceptions, it had occurred every night from March to December. The sexual functions seem to have been disturbed at the same time, the patient losing all sexual desire, and never having an erection of the penis. The account given by him in December, 1897, suggested overflow from a distended and atonic bladder rather than true incontinence. He said that, when he had passed water, more came on further effort; and that "coughing would then again cause the stream to flow out in jerks." The stream was at all times weak, and he passed water for about a quarter of an hour before going to bed, doing so while kneeling to say his prayers. It was at eight o'clock in the evening that he first came for advice, and a catheter was then passed. No stricture or other obstruction was found. A pint of urine was drawn off; it came fairly strongly at first, but for a long while at the end it merely trickled. The urine was acid, it contained albumen and pus, no casts were found. The albumen and pus disappeared later when the bladder had for some time been regularly emptied by the catheter and washed out at intervals.

Of other symptoms, the only one noticed at this time was some defect of vision. It caused him no serious inconvenience; but he noticed that there were spots in groups, before the right eye. The pupils were at this time normal in size and shape, and re-acted both to light accommodation. The muscular strength was good everywhere. Knee-jerks were present, but perhaps a trifle sluggish. He had occasionally sudden and brief pains in the legs. The tongue was rather red and had a swollen appearance.

After this he was not seen for two months, re-appearing in February, 1898. The "incontinence" had become less troublesome, but there was again pus and albumen in the urine, and he did not seem to know by his sensations when the bladder was over-distended. He went away for several months to the Riviera, and was next seen in November, 1898, after an interval of nine months. He was suffering at the time from a febrile attack, with temperature 101-102° F., the fever lasting for four days. He had no headache, did not complain of pain in his back or limbs, was listless and heavy, and inclined to wander in his talk. On recovering, he gave some account of his experiences during the preceding nine months, and a fuller examination was made of the nervous system. He said that he had been better during the summer, but thought that he had lost some strength. He had come to use the catheter regularly, and could not pass water without it. The pus and albumen were no longer present, there was some slight improvement in the force with which the urine was expelled through the catheter.

Examination revealed the following facts :—

(1) In common sensation there was nowhere any change from the normal.

(2) The sense of pain and the temperature-sense were very markedly affected. While in bed he had allowed both his feet to remain in contact with an uncovered hot-water bottle; and while he felt no pain, large burns had resulted. These healed slowly but satisfactorily. The accompanying diagram shows fairly accurately the degree of analgesia, and the regions affected. It was most marked over both legs below the knee. On the right leg in front, it ascended also

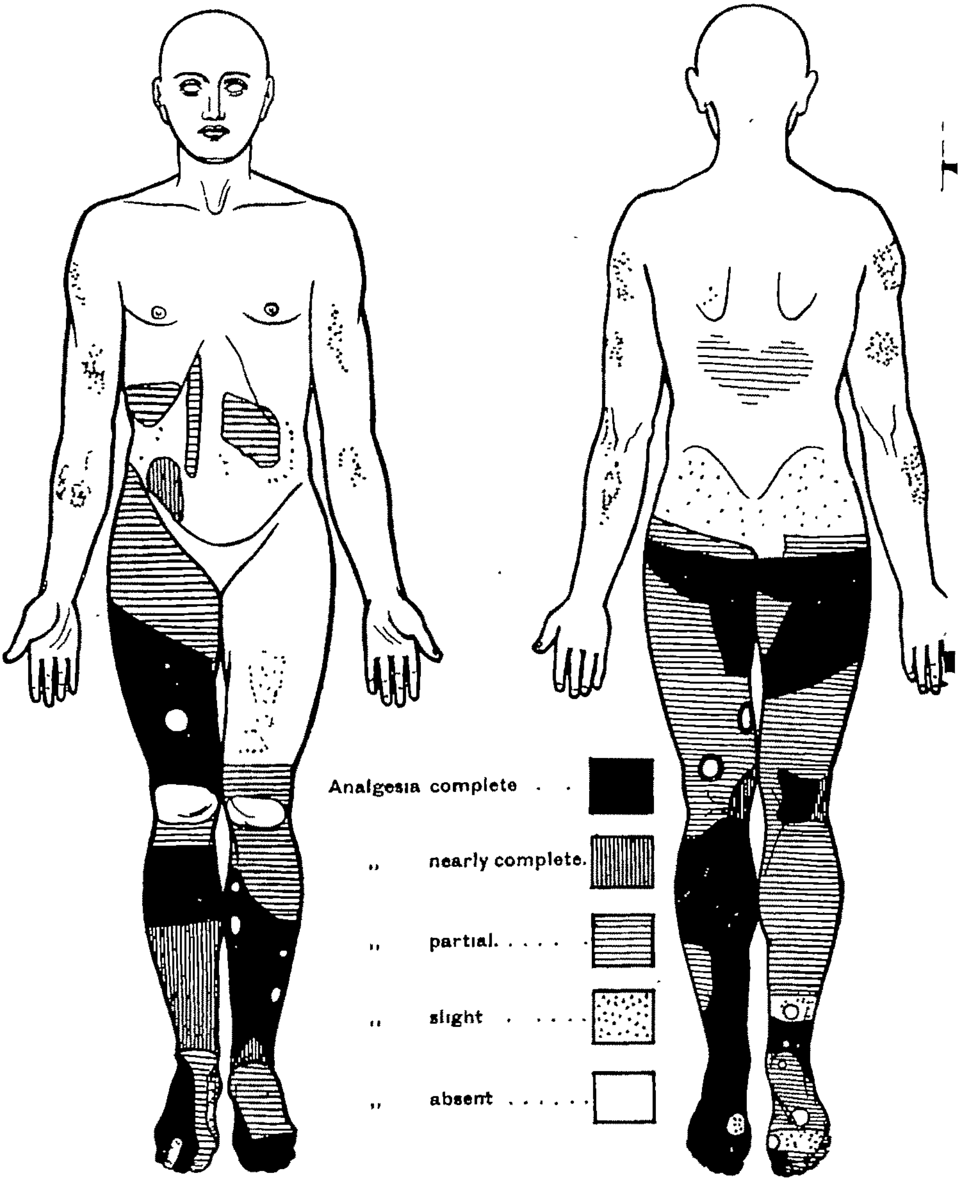


FIG. 1.—Diagram of areas of analgesia.

to the groin. It was traceable over part of the abdomen and, in a slight degree, over areas of the forearms and upper arms. On the posterior surface of both legs it extended in varying degree to the buttocks. In several places there were small patches of acute sensation surrounded by analgesic regions, as, for example, in front of both knees, in the front of the left leg, and on the soles of both feet.

(3) The knee-jerks were, as before, present but sluggish.

(4) The muscular power was certainly not below the average in any part of the body, though the patient complained that his muscles felt weak. There were no tremors.

(5) The smell and taste were normal.

(6) The sight of the right eye had become less clear. He complained much of a sensation as of dust moving in front of it. The light-reflex in this eye was sluggish. The pupil was smaller (*sic*) than that on the left side. The optic discs appeared normal, and no disease of choroid was observed; but there were marked opacities in the right vitreous humor, and the left was not quite clear.

(7) Shooting pains in the limbs had become more frequent. They occurred usually in the feet or toes, coming on suddenly without warning and being momentary but severe. He had occasional twitchings in the lumbar muscles.

(8) Drowsiness had become a marked feature of the disease during the last few months. He slept twelve hours out of the twenty-four, from eleven to eleven.

(9) The hearing was imperfect. At first he could hear a watch at 4 inches only on the right side, and 1 inch on the left. Some cerumen was removed: but this only caused an improvement up to 10 inches on the right, and 3½ inches on the left side. The membranes appeared normal.

Up to this time all the symptoms observed, with the exception of the drowsiness (and perhaps the eye and ear symptoms), were referable to the spinal cord; there were none of the brain-troubles—the aphasia and paralysis—that had been observed in the three elder brothers. The patient had also lived to a greater age than any of his brothers; and the disease had been observed in him for two years without making very rapid progress. But in March, 1899, he went out to a dance, and came home at three o'clock in the morning. He was unable to get a cab, and had to walk for two or three miles. Having been warned to avoid fatigue, he stayed in bed till one o'clock the next day; but while dressing he dropped a glass from his right hand, and found that he was unable to express himself clearly in words. He was seen by one of us within three-quarters of an hour of the commencement of the attack; the aphasia was then still marked, and he failed to read when asked to do so, no less than to converse. The attack had subsided an hour later, and he felt and seemed quite well in the evening.

He was again away, staying at Weymouth, during the greater part of the summer. On the whole, he had fair health while there; but in August (1899) he had two more attacks of temporary aphasia. Once also, after having been out in a boat (but without exposure to cold or wet) he was seized with severe pains in the folds of the buttocks, lasting about four hours. The pains came on about once a minute. He also had the afore-mentioned shooting-pains about once a month throughout the year, usually in the legs, sometimes in the hands. At the same time he gradually became weaker, and when seen in November (1899) had lost a good deal of flesh, especially in the lower limbs. The areas of analgesia were again mapped out, and were found to show very little variation from those of a year earlier. At this time, too, the eyes were examined by Mr. Lawford, who has kindly given us the following report on their condition.

October 16, 1899. Pupils dilated by homatropin and cocain.

$$\text{V.}\quad \text{R. } \tfrac{6}{36} \begin{smallmatrix}+\,0{\cdot}5\text{ sphl.}\\ -\,2{\cdot}0\text{ cyl.}\end{smallmatrix} = \tfrac{6}{24}.$$

$$\text{L. } \tfrac{6}{18}\text{ vix } \begin{smallmatrix}+\,0{\cdot}5\text{ sphl.}\\ -\,2{\cdot}5\text{ cyl. }15^{\circ}\end{smallmatrix} = \tfrac{6}{18} \times \tfrac{6}{12}\text{ tried.}$$

Fields of vision full. Ophthalmoscopically right and left no abnormal appearances detected in any part of fundus. Examination of right fundus much interfered with by vitreous opacity. Colour of O.D.'s healthy. Right cornea and lens clear. In vitreous there are numerous stringy, slowly moving opacities, chiefly about the middle of vitreous, antero-posteriorly. They are all dark in appearance: no whitish bands seen. There is also much fine dust-like haze of vitreous. Left.—The changes in vitreous are very similar, but MUCH less obvious. The stringy opacities are about middle portion, but are few in number. Fundus can be easily and clearly seen.

When examined on a previous date without a mydriatic, the pupils were unequal and irregular. Right pupil oval, long axis horizontal: size 4 mm. Left pupil pyriform, size 6 mm. Actions of pupils to light very sluggish, and very small in amount; to accommodation fair, but less extensive than usual. Ocular movements and lid movements full. Tension normal.

The relatives were at this time anxious to try the effect of general massage, having seen the improvement produced in our patient's younger sister by Weir-Mitchell treatment; and a course was arranged for him, special care being taken to prevent his being over-tired. He was not seen again for a month. During that time he had become very distinctly worse. He had had about six attacks of aphasia, usually accompanied by temporary weakness in the right arm. In spite of this, however, he went out three consecutive evenings, and on the fourth day was so much worse that a doctor was again summoned. When seen he had not fully recovered from an attack of the preceding evening, his speech being imperfect, and the right grasp weaker than the left. His general weakness was now very great, and he could not be up for one hour without feeling fatigue. His memory and power of concentration were both feeble; the pulse usually rapid (90-100), the tongue absolutely dry. He complained of pain in his limbs of an aching character: the temperature was normal or subnormal. With rest, careful feeding, attention to the state of the bowels, and skilled nursing, he gradually recovered a certain amount of strength; and the attacks of aphasia, at first occurring every day, became less frequent. By February 20, 1900, he had been as much as ten days without an attack, and was able to be up for four or five hours without fatigue. During the spring and summer yet further improvement followed, and, while carefully avoiding all that tended towards over-exhaustion, he was able to move about freely out of doors, and to mix in society.

During the remainder of his life, the patient was under the care of Dr. R. Jocelyn Swan, to whom we are indebted for the following notes of that period. He lived for about nine months longer, and during that time had four convulsive attacks, in the last of which he died. "The first convulsive attack," Dr. Swan writes, "occurred on September 26, 1900, and lasted about twelve hours. A second similar seizure was on November 3, more violent and longer in duration, in all thirty-six hours. A third occurred on January 15, 1901, lasting nine hours, this was marked by a tonic contraction of the left arm, while the right moved aimlessly about, and the final attack was on May 24, commencing at 1 a.m., and lasting till he died at 9 a.m. of the same day." Dr. Swan adds that he continued to have "lightning-pains," especially at night; the two regions most affected being a spot on the outer side of the right foot below and in front of the external malleolus, and the folds of the buttocks. In the beginning of March he also had an attack of conjunctivitis of the right eye, which had become nearly blind; and there was some ulceration of the cornea leaving a nebula. It is not known whether the cornea had previously become anæsthetic; or whether the analgesia previously observed had extended over a larger area of the body.

II.

PATHOLOGICAL NOTE.

The *post-mortem* examination was made seventeen hours after death. The weather at the time was very warm. *Post-mortem* rigidity was well marked. There was considerable discoloration and lividity in the dependent parts. The head was opened first and on removal of the skull cap the dura was seen to be intensely congested. The venous sinuses were full and when the brain was removed blood oozed in considerable quantity from the spinal canal. In exposing the spinal cord an abnormal density of bone in the vertebral laminæ was observed, notably in the lumbar region, and there was some extra-meningeal hæmorrhage in front of the cauda equina.

Thorax.

The heart was normal. The right lung was adherent at the apex from some old pleurisy, and in both it and in the left there was some patchy hypostatic consolidation and the lungs were markedly congested throughout. There was no sign of tuberculous disease.

Abdomen.

The liver and the spleen were both in a state of venous congestion.

The kidneys had their capsules readily separable and had also the appearance of congestion, though microscopically they seemed absolutely normal. The bladder was normal.

For microscopic examination, most of the organs were hardened in 10 per cent. formalin. Some of the cord, however, was placed in Müller's fluid.

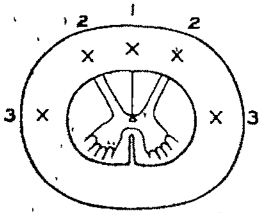
For the nervous system, the staining methods were those of Nissl, van Giesen, Marchi and Weigert-Pal, along with others.

Spinal Cord and its Coverings.

Macroscopic.—The dura showed marked congestion. On reflection of the dura a rusty-coloured substance was seen to be present between it and the cord. This was gelatinous, stringy and friable, and in consistence suggested a fibrinous exudate. It formed a more or less complete sheathing to the cord throughout its entire length. It was, however, most abundant in the lower parts of the cord and was less so as the higher levels were reached, being in the neck almost absent. It was found chiefly on the posterior aspect and in some regions it separated the dura from the cord to the extent of a sixth of an inch or more. Anteriorly it was seen mainly as stringy masses about the anterior nerve roots. It was moderately adherent to the dura, but more so to the cord itself, so that the former could without difficulty be raised, leaving the cord surrounded by its shaggy covering (fig. 2).

Microscopic.[1]—Examined under a low power. Sections taken from the level of the third cervical segment to the cauda equina all showed undue vascularity. This was not so striking in the cervical region, but got greater in lower levels, and became intense in lumbar and sacral regions. This vascularity affected chiefly the pial layer of the pia-arachnoid and the contents of the arachnoid space, viz., the nerve roots and the arachnoid tissue. But the vessels of the dura and the cord itself were also distended. The vessels seemed increased both in size and number. In the arachnoid space was a relatively large quantity of a fibrous material probably a hyperplasia of the normal fibrous trabeculæ. In general appearance it was similar to the fibres of the arachnoid tissue, but the cellular elements were fewer. It had the form of nodulated rods or fibres with a maximum diameter of about thirty times that of a red blood cell. There were also spheroidal bodies, though these probably were cross sections of the fibres. This tissue was found in different situations in the arachnoid space, among the nerve roots—sometimes actually among the nerve bundles of the roots—and more plentifully posteriorly.

There were usually aggregations of it in the following situations where normally a collection of arachnoid tissue might be expected:



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[1] The terminology is that used by Ford Robertson by which *pia-arachnoid* is taken to mean the whole membrane, "pia," "arachnoid," and intervening tissue: and *arachnoid* is taken to mean the trabecular tissue which extends from the outer to the inner aspect of the membrane, thus, arachnoid trabeculæ, arachnoid spaces, arachnoid fluid.

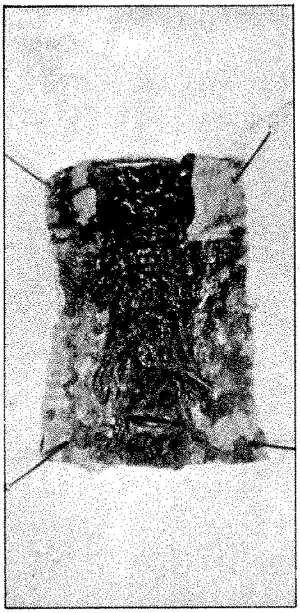

FIG. 2.—Portion of dorsal cord; posterior aspect, dura reflected.

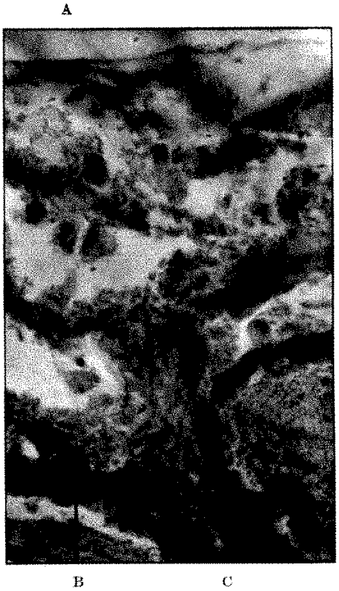

FIG. 3.—Photomicrograph. Mid-dorsal cord, transverse section, between posterior dura and cord (region about septum posticum). Hæmalum, × 105. *a*. Dura. *b*. Red blood cells. *c*. Arachnoid tissue.

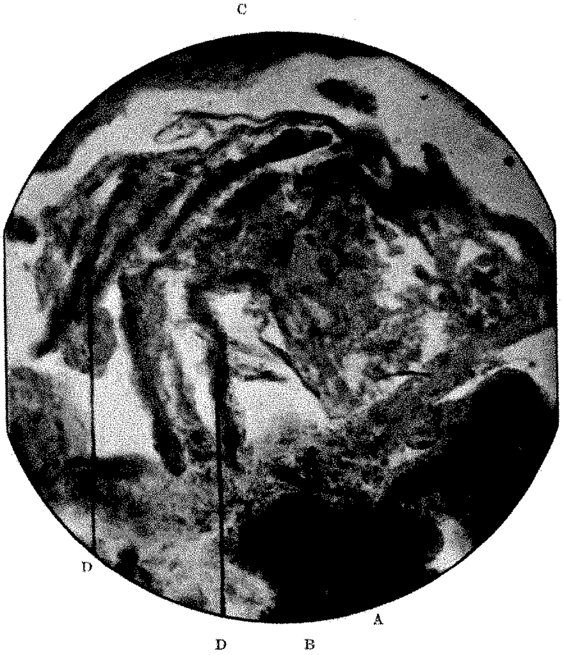

FIG. 4.—Photomicrograph. Lumbar cord, transverse section, mass of arachnoid tissue, opposite one of the posterior roots. Hæmalum, × 60. *a*. Engorged blood-vessel. *b*. Hæmorrhage. *c*. Dura. *d*. Arachnoid tissue.

An aggregation at 1, presumably the septum posticum, was found chiefly in the higher regions; an aggregation at 2, chiefly in the lower regions. At 3, the position of the ligamentum denticulatum, there was an aggregation in all regions. The material was also present in the neighbourhood of the anterior fissure.

The fibres of this tissue had no definite arrangement, except in the above-mentioned groupings, but were disposed in all directions forming in places a loose network (figs. 3 and 4).

Under a high power they were seen to be fibrillar and with Weigert's fibrin stain they gave negative results. In the cauda equina it was present chiefly near the dura, but it was also to be seen among the nerve roots. In the interstices of this tissue collections of red blood cells were everywhere abundant, especially in the lower levels of the cord.

Stratified bodies (geschichtete Körperchen) were found in considerable numbers near the dura. The pial layer of the pia-arachnoid was much thickened. Its vessels were engorged, and in places there were hæmorrhages. There was in it an extensive round cell infiltration which invaded also the periphery of the cord itself, especially along the lines of the connective tissue septa and was marked in the neighbourhood of the posterior roots (fig. 5). The nerve roots presented the same appearance of intense congestion and round cell infiltration, and these conditions, though to a less extent, were also evident in the dura. In several of the smaller arteries there was distinct thickening of the intima presumably endarteritis. This was evident throughout the whole length of the anterior median artery. Thrombosis seemed to have taken place in several of the vessels in the more highly congested areas, and some of the thrombi were apparently undergoing organisation. The endarteritis did not affect the whole intima equally, being usually seen in transverse sections as an encroachment on one side of the lumen of the vessel (fig. 6).

Treated with the Weigert-Pal and Marchi staining methods the cord showed a degeneration in the posterior columns.

In the lower lumbar region the degenerated fibres were found mainly in the postero-external columns, but gradually as one passed up the cord they became more and more strictly limited to the postero-median columns. The degenerated fibres extended anteriorly in the postero-median columns as far as the gray commissure, except in the cervical region, where they only reached about one half of that distance. It was in fact exactly such a degeneration as would be occasioned by damage to the lower lumbar and sacral roots. In addition to this there was a marginal degeneration all round the cord, and extending to the parts bounding the anterior fissure (fig. 7).

Sections through the upper part of the cauda equina treated with the Weigert-Pal method showed many of the roots much degenerated.

The nerve cells in sections taken at many levels of the cord treated by Nissl's method, appeared absolutely normal. There was no evidence of chromatolysis or other degenerative change. The chromophile substance, as represented by the "Nissl-bodies" seemed normal in quantity, arrangement and staining reaction. This applies to cells in all situations—in anterior and lateral horns and Clarke's column. In a few cells there was a deeply staining nucleus, but this was taken to be a *post-mortem* change. Beyond engorgement, the vessels of the cord itself were not affected. There was no perivascular round cell infiltration. Concentric bodies, giving "amyloid reaction," were present in the white matter in moderate numbers.

Brain and its Coverings.

Macroscopic: The dura showed great congestion. It being reflected, the surface of the brain was seen to be intensely congested, especially over its convexity, while covering the medulla and base of brain, was found what appeared to be the same gelatinous, friable substance already described as surrounding the cord. The pia-arachnoid was cloudy and thickened over Sylvian fissures, and on opening up the latter, the same substance was found filling them up and causing the two sides to be adherent.

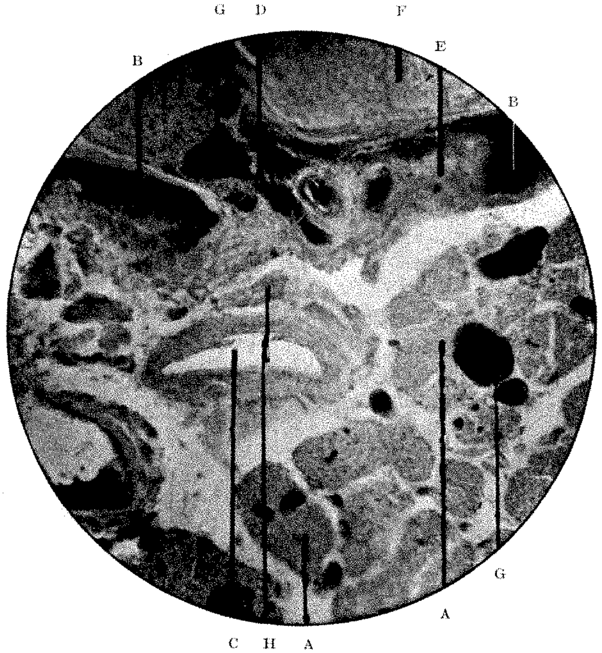

FIG. 5.—Photomicrograph. Sacral cord, region about anterior fissure. Hæmalum, × 60. *a.* Nerve roots. *b.* Dilated blood-vessels, possibly hæmorrhage. *c.* Artery with thickened intima. *d.* Inflammatory infiltration in anterior fissure. *e.* Thickened pial layer of pia-arachnoid. *f.* White matter of cord. *g.* Dilated blood-vessels. *h.* Arachnoid tissue.

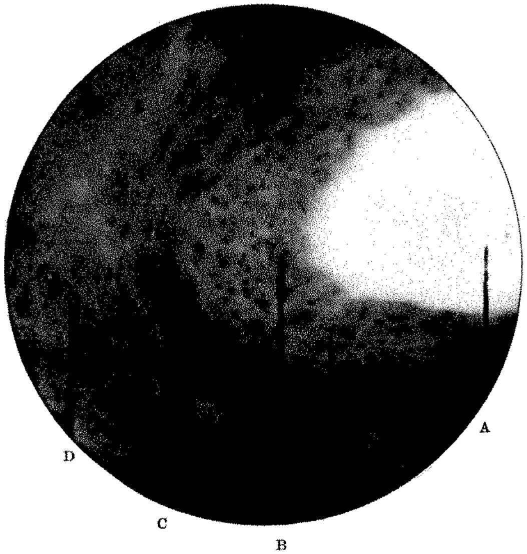

FIG. 6.—Photomicrograph. Lumbar cord, transverse section of anterior median artery. Hæmalum, × 270. *a.* Lumen of vessel. *b.* Thickened intima. *c.* Media. *d.* Adventitia. N.B.—This appearance is not due to obliquity of section.

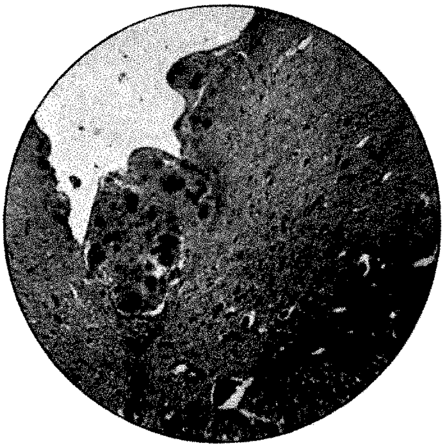

FIG. 8.—Photomicrograph. Floor of fourth ventricle in pons, showing "hyaline" bodies, Van Giesen, high power.

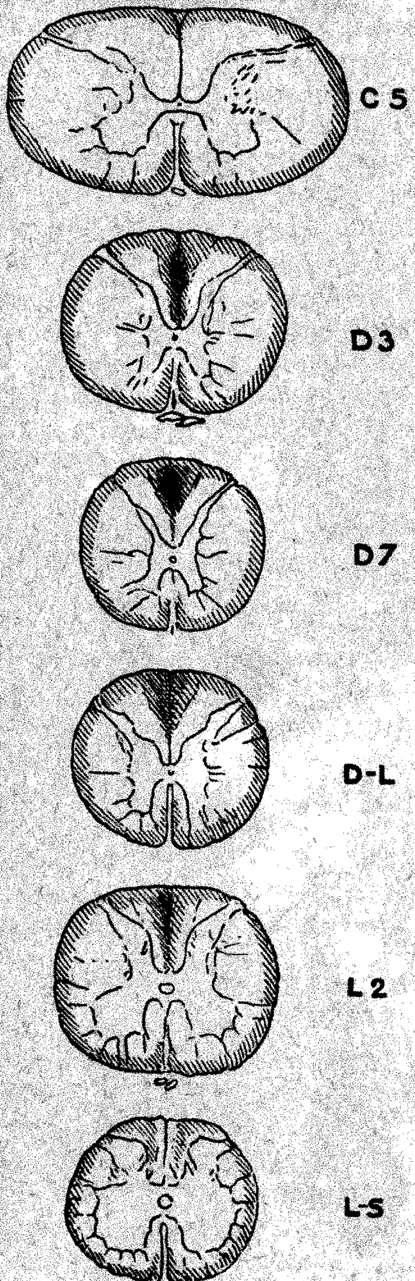

FIG. 7.—Drawing from sections prepared by the Weigert-Pal method to show cord degeneration.

It was also present between the two frontal lobes below the corpus callosum, making them adherent, and surrounding the anterior cerebral arteries and their branches. The pia-arachnoid did not separate easily from the cortex. In all other respects, the brain appeared quite normal. The left Sylvian artery with its main branches contained clot, but this was red and non-adherent, and probably *post mortem.* Recent clot was present also in several other branches of the circle of Willis.

Microscopic.—Sections were made through Basilar artery, both Sylvians, both anterior cerebrals and posterior communicatings. All were found perfectly normal with the exception of the first, which showed very slight endarteritis.

Sections of the third left frontal convolution, and of many other parts of the cortex were examined. There were practically the same appearances in all. There was a fibrous hyperplasia of the arachnoid tissue, with increased vascularity. The cortical arterioles were normal. The cortical nerve-cells were likewise normal, examined by Nissl's method. Many however, had the deeply staining nucleus and indistinct chromophile substance, described by Ford Robertson as *post-mortem* change.

Sections of the left internal capsule and of the corpora striata were also examined with portions of the white matter from various other regions, and all seemed quite normal.

Sections through the medulla and pons showed the nerve-cells at the floor of the fourth ventricle normal, and the same appearance of the pia-arachnoid, as was seen on the cord.

In the medulla and pons, immediately subjacent to the ependyma lining the fourth ventricle, were numerous, roundish, homogeneous, hyaline-looking bodies with concentric markings, not staining very deeply with methylene blue, and about ten or fifteen times the diameter of a red blood cell. These bodies did not blacken with osmic acid, nor did they give the "amyloid reaction" with iodine, or iodine and sulphuric acid (figs. 8, 9, 10).

These bodies were not present under the ependyma of the lateral ventricle. The cerebellum was normal.

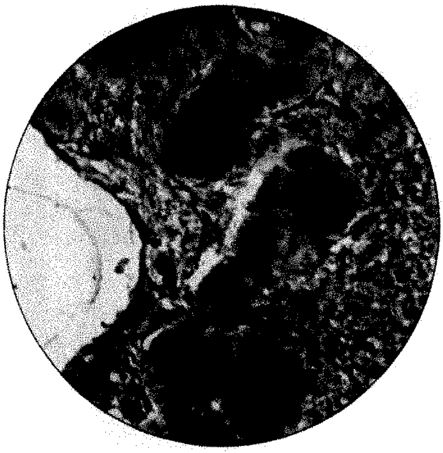

FIG. 9.—The same, low power.

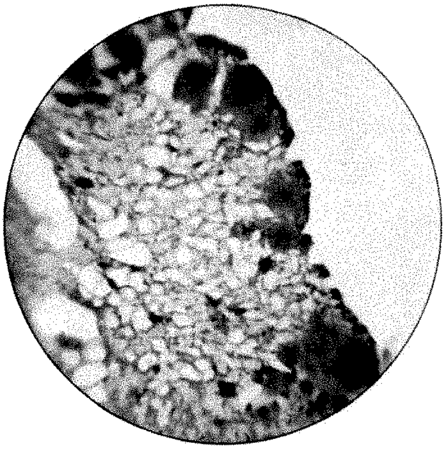

FIG. 10.—Photomicrograph. Floor of the fourth ventricle in medulla, at level of hypoglossal nucleus, showing "hyaline" bodies, Van Giesen, × 370.

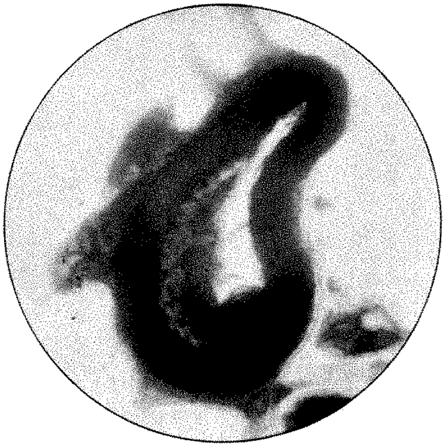

FIG. 11.—Photomicrograph. Artery from great sciatic nerve, showing thickened intima. Hæmalum, × 270.

Peripheral Nerves.

The peripheral nerves as represented by the ulnar and great sciatic were examined by the Marchi and Weigert-Pal methods, and were found to be normal, showing no sign of either neuritis or degeneration. Some of the arteries, however, in the great sciatic had the same thickened intima already described in the vessels of the cord (fig. 11).

The Eye.

The right eye was embedded in celloidin, and it was examined in antero-posterior sections. There was no direct evidence of choroiditis, but in the posterior chamber there was a considerable quantity of filmy, fibrinous looking material. The eye in other respects appeared normal.

The condition thus seems to have been primarily a spinal, lepto-meningitis extending from below upward until the cerebral meninges were affected in a like manner, chronic in its course, but intense enough to implicate the cord superficially, and many of the nerve-roots in the inflammatory process.

The great vascularity and numerous hæmorrhages in the inflamed area suggest an inflammation hæmorrhagic in type, and the excess of arachnoid tissue suggests that this constituent of the pia-arachnoid was especially involved.

The tract degeneration in the cord is manifestly the result of damage to the lower posterior roots. The bodies in the floor of the fourth ventricle are not fatty, and not amyloid as is seen by their staining reaction. They seem to belong to the group of hyaline bodies.

Our best thanks are due to Dr. Lazarus-Barlow for many kind suggestions, and for allowing us to make use of the pathological laboratory of Westminster Hospital during the preparation of this part of our paper.

We have found among other works the following of particular service :—

KEY AND RETZIUS. "Studien in der Anatomie des Nervensystems, &c."
OBERSTEINER AND HILL. "Anatomy of Central Nervous System."
FORD ROBERTSON. "Pathology of Mental Diseases, 1900"; and "Normal and Pathological Histology of Nerve-Cell," BRAIN, 1899.

POLLACK (JACK). "Methods of Staining the Central Nervous System," 1899.

MOTT. "Tabes dorsalis"; Clifford Allbutt, "System of Medicine," vol. vii.

III.

Before considering the nature of the disease we may here review shortly some of the more prominent symptoms, and consider in what degree they may be accounted for by the lesions above described.

(1) *The Bladder Symptoms* occurred in three out of the four males who suffered from the disease. With regard to the three females of the earlier generation no mention is made of this symptom, but the records concerning them are not full enough to justify us in concluding from this that the bladder was unaffected. Usually the nocturnal escape of urine was the first symptom in the disease to attract the attention of the patient himself, and in the earlier stages of the male cases it was regarded as an isolated symptom, like the incontinence of children, and treated with belladonna, &c. Later, however, the bladder becomes undoubtedly atonic, urine is retained in the bladder, and cystitis is set up, and in the light of the fuller knowledge of the last case that we now possess there can be little doubt that the primary defect is *retention* due to some fault in the nervous mechanism of micturition.[1] When we first saw our patient the bladder walls had already become very considerably weakened. He could expel very little urine with any force, the remainder trickling slowly away; the catheter showed several ounces of residual urine, after the first free flow of urine had ceased; pus and albumen were present, and disappeared when the bladder was regularly washed out. At this time he was having what he called "incontinence of urine" every night, and the most probable cause for this is that the bladder was only half empty when he went to bed, in a few hours it became full to its utmost capacity, and then discharged a certain portion of its contents, either by

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[1] J. RISIEN RUSSELL (Clifford Allbutt "System of Medicine," vi., 877), says that in affections of the spinal meninges retention is common, incontinence also occurs, though more rarely.

reflex stimulation of the lumbar centre or by simple overflow. Later in the disease all power of voluntary micturition was lost, and the bladder was emptied at regular intervals by the catheter, this prevented over-distension from occurring, and the so-called incontinence now disappeared. Three nervous lesions suggest themselves as possible causes for this retention:

(1) Disturbance of the lumbar centre for micturition.

(2) Disease of the white fibres in the lumbar or dorsal region, carrying impulses from the brain to the centre.

(3) Analgesia of the bladder, similar to that existing in the legs, allowing distension to occur frequently without discomfort, and in time to weaken the muscular fibres of the bladder wall.

(1) *Disturbance of the Lumbar Centre.*

The cord has suffered considerable damage in the region of the lumbar enlargement, enough possibly to account for imperfect action of the centre, and this explanation of the symptom is tempting, inasmuch as similar damage to neighbouring centres would account both for the constipation and for the loss of sexual power. But the early symptoms suggest that the centre is cut off from the usual stimuli rather than that it fails to act in response to them, and the later stages of disease of the centre should cause paralysis of the sphincter, with continuous overflow, rather than retention.

(2) *Disease of the Descending Tracts above the Lumbar Centre.*

A lesion of this nature would cause retention of urine, and a series of symptoms not unlike those observed; but no such lesion has been discovered on examination of the cord; and the absence of discomfort when the bladder was distended is hard to explain. It is possible, however, that this might be attributable to further damage elsewhere, *e.g.*, in the posterior roots.

(3) *Analgesia of the Bladder Wall.*

A failure to perceive the pain and discomfort normally felt when the bladder is over-distended might lead to a condition such as has been described; and it is known that retention sometimes occurs in syringomyelia.[1] If, however, the cause lies here, it will, no doubt, have been at work long before the first escape of urine; indeed, dissociated anæsthesia will be the first symptom of the disease. The sequence of events would be as follows:—The patient allows his bladder to be over-distended on many occasions without feeling the discomfort that would trouble a healthy man;[2] the bladder becomes distended, weakened, atonic; then it is incompletely emptied, and cystitis occurs. Finally, it loses all muscular power, and no longer responds even to the reflex stimulus of great distension.[3]

It does not seem impossible that more than one of these agencies may have been effective in producing the symptoms described.

Opacity of the Vitreous Tumour of the Eye.

This was present in two out of the three patients in the earlier generation, and in two out of the five in the later generation; while in the others we have no record as to the presence or absence of the trouble. The constant lesion consists in vitreous opacities, the appearance of which has been carefully described for us by Mr. Lawford; almost complete blindness may follow, as occurred in the mother of patient. A variation in the size and shape of the pupils has also been observed in the latest of the cases. No hæmorrhages within the eyeball have at any time been seen, and no choroiditis was observed in that part of the choroid that can be examined with the ophthalmoscope; but it is most probable that the primary cause of the opacities is hæmorrhagic, and it is possible that disease may have been present in the anterior portion of the choroid, or other parts of the uveal tract, though, as has been pointed out, no evidence of this was found microscopically.

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[1] Ref. WALTER VOUGHT, "Syringo-myelia and Allied Diseases." *N.Y.M.J.*, November 21, 1891.

[2] It is possible that the penile pain felt a week before the first voluntary escape of urine was caused by great pressure on the neck of the bladder, which still retained some pain sense.

[3] J. RISIEN RUSSELL (Clifford Allbutt "System of Medicine," vol. vi., p. 877) has described residual anæsthesia as being especially common in the bladder and rectum in affections of the Spinal Meninges.

The disturbance of the sense of heat and pain, along with unimpaired tactile sensation, seems to point to the probability suggested by Gowers[1] that the paths of conduction of heat and pain sensation are close together, but are widely separated from the path conducting tactile impressions.

It has been suggested by Starr[2] that on their way from the surface of the body the sensations of heat and pain traverse the gray matter and then go on in the centripetal fibres of the antero-lateral-ascending tract of Gowers. If this is so it might well be that the disturbance of heat and pain sense was due to the implication of this tract in the marginal myelitis which we have seen to be present, the gray matter being to all appearance normal.

With regard to the cerebral symptoms, drowsiness, impaired hearing, aphasia, right-sided hemiplegia, loss of memory and power of concentration, convulsive attacks and coma, we would suggest that they were due to a condition of cerebral anæmia caused, in the first place by venous congestion associated with the inflamed meninges interfering with the normal arterial blood supply; and in the second place by actual compression of the arteries by the new inflammatory material.

The latter might account for any local increase of the anæmia, such as that capable of causing aphasia or hemiplegia, and indeed the quantity of new material found in the Sylvian fissures and elsewhere at the base of the brain, matting everything together, makes this hypothesis not very improbable.

This does not, however, explain the transitory nature of the attacks of aphasia and paralysis.

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[1] "Diseases of the Nervous System," vol. i., pp. 235, 287.

[2] Clifford Allbutt, "System of Medicine," vol. vii.

Finally, a few suggestions may be made with regard to the nature of the disease, which we have described. We think that it will be admitted that the consistent grouping of symptoms is sufficiently marked to constitute the disease a definite entity; and that in character it corresponds to no form of hereditary nervous disease that has hitherto been described.

There is, however, a superficial resemblance to some of the known diseases Thus, it resembles syringomyelia in the one symptom of dissociated anæsthesia; and it is also like this disease (as well as certain other hereditary affections, *e.g.*, hereditary chorea, hereditary cerebellar ataxy, and hereditary ataxic paraplegia) in the late onset of the symptoms, after a healthy childhood and youth. There is a closer resemblance to locomotor ataxia in the lightning-pains, the diminution of knee-jerks and of light-reflex, and in one actual lesion found *i.e.*, the posterior sclerosis (though this symptom in our case was presumably secondary to the pia-arachnitis): while both locomotor ataxia[1] and Friedreich's ataxia[2] may be accompanied by dissociated anæsthesia and impairment of the sexual and bladder functions.

Now there is strong reason to believe that there is a close connection between locomotor ataxia and syphilis and the pathological evidence that has arisen in the investigation of the last case suggests the possibility of the disease being caused by the action of the virus of hereditary syphilis on the structures surrounding the spinal cord. The likelihood of this factor was considered during the lifetime of the patient; but was put aside because no satisfactory evidence existed that syphilis could involve three successive generations;[3] but that this objection is not final must be admitted in consideration of the following facts:—

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[1] Clifford Allbutt, "System of Medicine," vii., 116.

[2] "Gowers," 1892, 1st Edit, 464.

[3] J. HUTCHINSON (Clifford Allbutt, "System of Medicine," ii., 263) says that no facts have yet been published on this subject. Out of eight families investigated in which the parents had suffered from hereditary syphilis, there were no syphilitic offspring "with one doubtful exception." He adds, however, that "several surgeons have expressed the belief that the influence of syphilis once acquired may be felt through several subsequent generations."

(1) The vascular pia-arachnitis, closely resembling that found in syphilitic meningo-myelitis.[1]

(2) The thickening of the tunica intima in some arteries similar to that found in syphilis.

(3) The ocular lesions, which suggest former hæmorrhages like those of syphilitic choroiditis.

(4) The thickening of the neural arches in the lumbar region, found at the *post-mortem* examination.

(5) The character and duration of the disease from which the grandfather died ("gangrene" of lung lasting four months), and his dissipated life.

(6) The frequent occurrence of temporary attacks of aphasia in cerebral syphilis.

(7) The diminution of pain-sense and temperature-sense,[2] common in syphilitic meningo-myelitis.

We therefore suggest that this may be yet another manifestation of this polymorphic disease; though it is impossible to say why the virus should have selected these special regions, while producing none of the better-known symptoms that accompany the hereditary form of the disease.

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[1] *Vide* OPPENHEIM (Mayer) "Text-book of Nervous Diseases"; RISIEN RUSSELL, Clifford Allbutt, "System of Medicine," vi.; ZIEGLER, "Special Path. Anat.," &c.

[2] Clifford Allbutt, "System of Medicine," vi., 895.

CASE OF EXTERNAL SPINAL PACHYMENINGITIS, IMPLICATING THE ENTIRE VENTRAL SURFACE OF THE SPINAL DURA.

BY CHARLES K. MILLS, M.D.
Clinical Professor of Nervous Diseases in the University of Pennsylvania,

AND

WILLIAM G. SPILLER, M.D.
Assistant Clinical Professor of Nervous Diseases and Assistant Professor of Neuropathology in the University of Pennsylvania.

From the William Pepper Laboratory of Clinical Medicine; Phœbe A. Hearst Foundation.

EXTERNAL spinal pachymeningitis, except the tuberculous variety of limited extent, is uncommon, and, so far as we know, no case of external spinal pachymeningitis is on record in which the entire ventral surface of the dura, from the foramen magnum to the caudal end of the dural sheath, was adherent to the bodies of the vertebræ by fibrous proliferations, and the rest of the spinal dura was normal. Such a case forms the subject of this paper.

A man, white, 42 years old, piano-tuner by occupation, was admitted to the Philadelphia Hospital, February 17, 1896. No family history of importance was obtained except that two brothers and three sisters died in childhood. The patient had been blind since he was three months old. During his early life he had scarlet fever, pneumonia, typhoid fever, and rheumatism. He drank moderately, and denied venereal disease.

In June, 1895, he, for the first time, had a feeling of numbness in the right great toe. This numbness, after gradually spreading to the knee, attacked the other foot and leg in the same way. He had no pain, but the numb limbs felt as if asleep. Previous to the numbness he had had, for a time not fixed, some swelling and tenderness in the legs, and an aching pain in the lumbar region. He could walk until November, 1895, but his knees became bent (probably from spasticity), and he felt as if walking on springs. He began to have nocturnal incontinence of urine in July, 1895.

On February 21, 1896, a few days after admission, the record was made of exaggerated reflexes in the lower extremities, with a tendency towards a spastic condition. Ankle clonus was marked in both feet. It is to be inferred that the condition noted as having developed between July and November, 1895, was still present, namely, numbness in the lower extremities, inability to stand and walk, and incontinence of urine. His heart and vessels were described as normal, lung expansion was good, and respiratory murmur was normal. His bowels were constipated. On October 12, 1898, a note was made that sensation was intact, that the knee-jerks were plus when the muscles were relaxed, and that ankle clonus was not present, possibly on account of rigidity. Ward notes made on November 29, 1900, stated that the legs became rigid on effort; the patient could extend his lower limbs and stand, but could not walk; the knee-jerks were excessively exaggerated, and the irritation, in taking this reflex, provoked spasms of the legs in extension. Both legs also became firmly adducted; the feet were spastic at the ankles; no ankle clonus could be elicited; the Babinski reflex was typical and decided on both sides; sensation was everywhere well preserved; the legs appeared to be hypersensitive.

On April 17, 1901, it was noted that his right hand had been cyanotic and painful for some time. Signs of gangrene began to appear on two fingers of the hand. The patient was transferred from the nervous wards to the surgical wards for treatment. As the gangrene was evidently spreading, and as the patient suffered excruciating pain, amputation of the right hand was performed April 18, 1901. So far as the operation was concerned the patient in all respects did well. On May 9, 1901, he complained of severe pain in the left side, and auscultation revealed some suggestion of a friction sound. The temperature rose, and pulse and respiration increased. On the 10th dulness over the left lobe was observed, and breathing sounds were harsh. His active lung symptoms gradually subsided, and he was retransferred to the nervous wards. On June 22, 1901, he again complained of pain in the left side. On examination a fairly superficial friction rub was heard in the mid-axillary line on the left side, from about the fifth to the seventh rib. At the angle of the left scapula was an area in which expiration was shortened and harsh. The whole left base was dull and breathing sounds and expansion were much decreased; fremitus was not markedly altered. The patient's pulmonary condition again improved, and he remained in fair health until December. He was troubled from time to time with dyspnœa, and in October had an attack of copious hæmoptysis. On December 7, 1901, he was attacked with severe dyspnœa. Breathing was laboured and frequent, and speaking was difficult. Expansion was limited on both sides. He grew rapidly worse, and died on December 8, with œdema of both lungs. The symptoms referable to the nervous system remained practically the same during the last year or two of the man's life. He was frequently seen by one of us (Dr. Mills) during his term of service. The patient's condition from the notes already given and from recollection can be summarized as follows: He was paralysed in both lower extremities, and these were the seat of spasticity and marked contractures; all the deep and superficial reflexes in the lower extremities were much exaggerated, and he suffered from incontinence of urine; objective sensation was everywhere intact as late as November 29, 1900.

The necropsy was made December 8, 1901. It revealed many interesting pathological conditions in various parts of the body which, with the exception of the condition of the spinal dura and spinal cord, need only be briefly summarized here as follows: Thrombosis of the right pulmonary artery, cardiac dilatation, miliary tuberculosis and œdema of the lungs, parenchymatous nephritis and arteriosclerosis.

The external surface of the spinal dura on the ventral

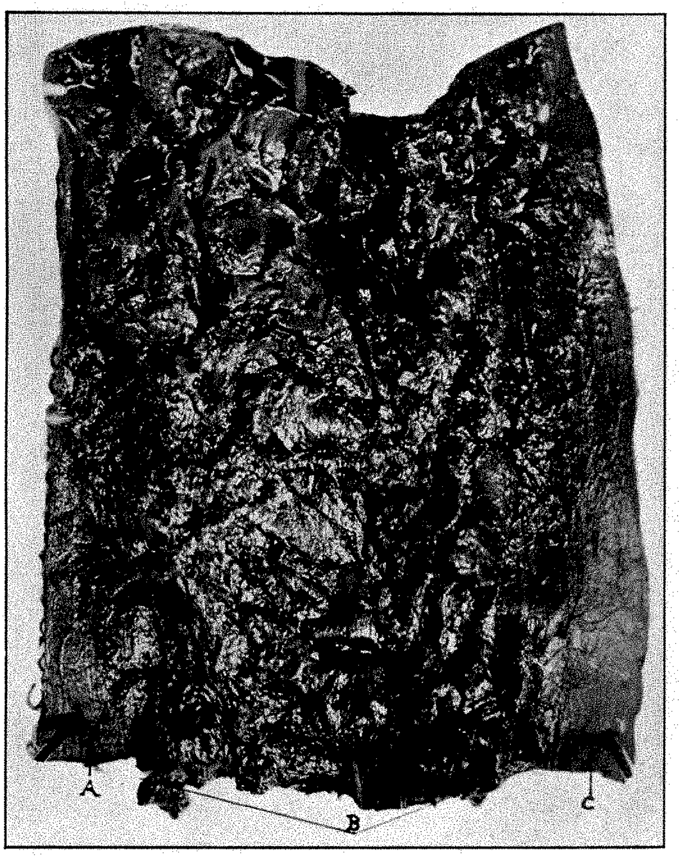

Fig. 1.

Photograph of the external surface of a part of the spinal dura.

The dura has been cut through in the dorsal portion. *A.C.* Dorsal portion of dura. *B.* Ventral portion of dura showing proliferation.

aspect was firmly adherent to the bodies of the vertebræ throughout the spinal canal. The dorsal aspect of the dura presented nothing abnormal, a single transection of the cord made between the tenth and the eleventh thoracic roots showed a gelatinous appearance to the naked eye in the crossed pyramidal tracts.

Microscopical examination reveals the following conditions:—

Sections from the right and left paracentral lobules appear to be normal, as do also sections from the medulla, except that the blood-vessels are distended.

Most of the nerve-cell bodies of the lower cervical region are well developed, although some appear atrophied, and here and there a few nerve-cell bodies in which the nucleus is displaced are found. Some small hæmorrhages of recent date are seen within the sections. The columns of Goll in the cervical region are much degenerated, and the degeneration is such as results from a lesion lower in the spinal cord. The ventral and dorsal roots appear to be normal. The direct cerebellar tract and the tract of Gowers on each side are degenerated. The crossed pyramidal tracts contain a slight excess of neuroglia, but by Weigert's hæmatoxylin stain do not appear degenerated. No signs of leptomeningitis are detected.

In the mid-thoracic region the degeneration is very intense, especially in the peripheral portions of the cord. Only the nerve-fibres near the central gray matter are intact. The anterior and posterior roots do not stain well, partly on account of the method of hardening, and it is difficult to decide concerning the condition of these roots. There is no evidence of leptomeningitis.

In the lumbar region the nerve-cell bodies seem to be normal. The crossed pyramidal tracts are degenerated, and the degeneration extends forward at the periphery of the cord, beyond the usual area of these tracts. The posterior columns are also partially degenerated. The condition of the anterior and posterior roots cannot be positively determined, as the roots do not stain well.

The dura, in its ventral portion, is composed of the fibrous tissue commonly found in this sheath, and the proliferations on the outer part of the dura are composed chiefly of the same fibrous tissue. At one place a small collection of cells with round nuclei, separated into groups by bands of fibrous tissue, is found, but collections of these cells with round nuclei are rare in the proliferations from the dura, and there is little evidence of acute inflammation. At some places what appears to be metastatic bone formation is found in the proliferations on the dura.

One of the ulnar nerves contains much excess of connective tissue between the nerve-bundles, and some of the nerve-bundles are partially degenerated. One of the musculospiral, one of the median, and one of the plantar nerves are in a similar condition.

A piece of muscle from the sole of the foot appears considerably atrophied, and numerous round nuclei are found in places between the muscular fibres, so that in these places myositis existed.

The eyeballs were examined by Dr. E. A. Shumway, whose report is as follows: "The smaller eye shows phthisis bulbi, with extensive bone formation in the interior of the eye, in the exudate on the choroid; nerve atrophic. The larger eye shows thick leucoma of cornea, staphyloma beginning; cornea entirely cicatricial; iris and ciliary bodies atrophied to a high degree; iris adherent to cornea throughout; organised tissue anteriorily due to old choroiditis; retina and choroid show chronic inflammation, with secondary pigmentation of the retina; optic nerve head deeply excavated, entirely atrophic."

Chronic external pachymeningitis of the cerebral dura is so rare that Alexis Thomson,[1] in 1894, said he had not been able to find the record of any specimen but that of the two which had come under his own observation. Lannelongue he mentions as having met with the condition while performing craniectomy in a case. One of Thomson's cases was in a child aged five years, who had died of abdominal tuberculosis. There was no sign or history of rickets or syphilis. The dura was firmly adherent to the calvarium,

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[1] ALEXIS THOMSON, *The Journal of Pathology and Bacteriology*, vol. ii., 1894.

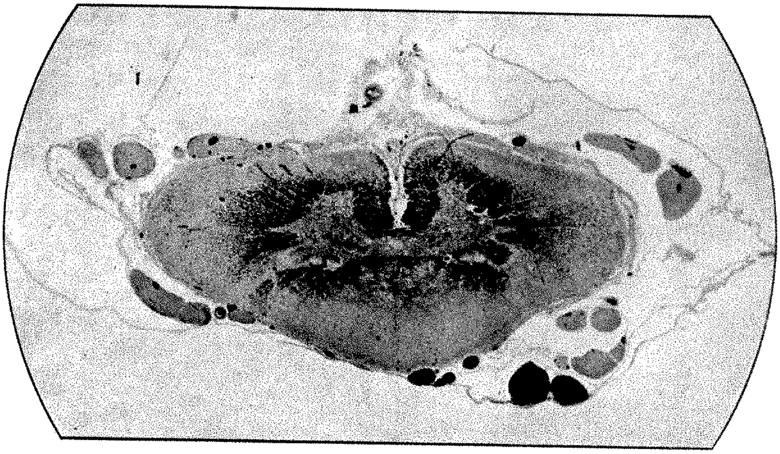

FIG. 2.

Photograph of a section from the mid-thoracic region.

The degeneration is intense in the peripheral portions of the cord.

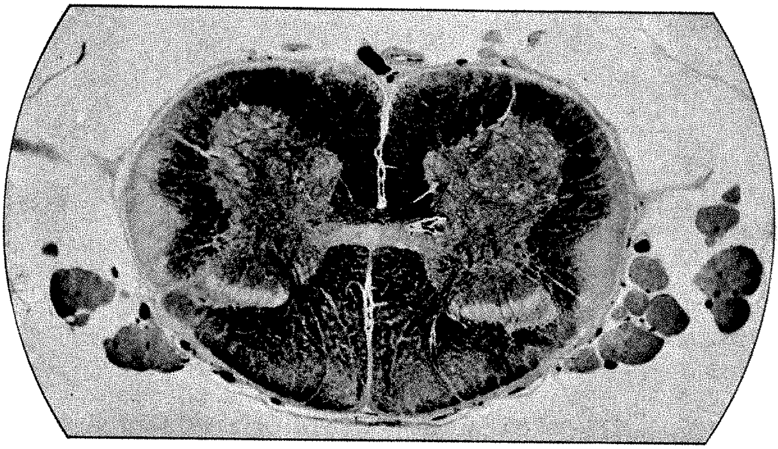

FIG. 3.

Photograph of a section from the lumbar region.

The crossed pyramidal tracts are degenerated, and the degeneration extends forward beyond the area of these tracts. The posterior columns are also partially degenerated.

and on being forcibly torn from the bone presented on its outer surface a uniform layer of red sprouting granulations or villous processes. The inner table of the skull presented an infinite number of grooves and pits in which the granulations were embedded. The lesion was confined to the outer aspect of the dura in the region of the parietal eminences, and was perfectly symmetrical on the two sides, the cerebral surface of the dura being normal. Each process on the outer surface of the dura was made up of one or more capillary loops, surrounded by numbers of cells, the majority of which were leucocytes. Among these were a few scattered spindle-shaped corpuscles, and here and there clumps of red blood corpuscles. The cells and vessels were feebly supported by a very delicate recticulum of fibrin.

The second specimen was found by Thomson in a museum.

Thomson believed that the characteristic features of the pathological process in these cases depended upon a reversal of the normal function of the dura, regarded in its capacity as an internal periosteum of the skull. Bone formation was replaced by the projection of vascular loops from the dura against the bone, leading to progressive softening of the latter, and the process was exactly like the method of absorption met with in inflammation (periostitis and osteomyelitis). Thomson says it was noteworthy that while the external surface of the dura was thickly studded with vascular granulations, there was scarcely any evidence of increased vascularity or of inflammatory changes in the substance of the dura. He regards the process as an aberration of development rather than as an inflammation. It caused no symptoms and showed no evidence of its existence during life.

External spinal pachymeningitis of non-tuberculous nature of limited extent has been occasionally observed. Stoubell's,[1] for example, reports a case of syphilitic external spinal pachymeningitis. A woman, aged 86, during one night became paraplegic in both lower limbs, and was anæsthetic as high as the umbilicus. The patellar reflexes were absent, and there was no ankle clonus. Death occurred two and a half weeks later from pneumonia. At the necropsy the thoracic vertebræ from the third to the sixth were found diseased, and the meninges in this region were thickened. A microscopical examination showed that the process was neither tuberculous nor carcinomatous. The meningeal growth had its origin from the outer surface of the dura, and was anteriorly united with the periosteum of the vertebral canal. It consisted of small-cell granulation tissue. The process was believed to be syphilitic. Stoubell remarks that syphilitic external pachymeningitis (peri-pachymeningitis) is extremely rare, and refers to cases reported by Virchow and Heubner.

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[1] STOUBELL, *Neurologisches Centralblatt*, 1898, p. 1, 120.

In the case described in this contribution, no disease of the vertebræ, to explain the adherence of the spinal dura to the bodies of the vertebræ, could be found at the necropsy, although no vertebral bodies were removed, and yet this adherence was so great that a knife was constantly employed to cut through the proliferation during the removal of the spinal cord and dura, and these proliferations consisted of dense fibrous tissue.

The degeneration of the posterior columns was probably caused in part by the degeneration of the posterior roots which were doubtless compressed by the abnormal fibrous tissue on the outer surface of the dura. Internal pachymeningitis or leptomeningitis did not exist anywhere. The intense degeneration of the thoracic region, especially of the mid-thoracic region, is difficult to explain. The spinal cord in the mid-thoracic region was very small, and the peripheral portions were entirely degenerated. The vertebral canal in the thoracic region is smaller than in the cervical or lumbar region, and if there were any œdema of the spinal cord, or any increase in the amount of the cerebro-spinal fluid, the effect of this pressure on a spinal cord firmly adherent by its dura to the bodies of the vertebræ might be most distinct in the thoracic region. The changes of the spinal cord in this region were such as might be produced by interference with the circulation and by pressure, and yet the nature of this pressure is not very evident, as the adhesions alone were hardly sufficient. The degeneration of the white columns of the cervical region was secondary to that of the thoracic region, as was also in part that of the lumbar region.

The degeneration of the peripheral nerves was probably caused by the involvement of the nerve-fibres, in passing through the thickened dura.

We cannot determine the nature of this external spinal pachymeningitis. There was very little evidence of acute inflammation, and the tissue forming the proliferations was chiefly of a fibrous character, and resembled closely that of the dura. It is possible that the process was syphilitic; but, if so, it was of a character very unlike that usually found in syphilitic lesions. Syphilis, when it occurs within the vertebral canal, usually causes a meningomyelitis, but there was not the slightest evidence of such a process in this case. The characteristic lesions of tuberculosis were not found within the vertebral canal. The external spinal pachymeningitis probably existed some time before it caused symptoms.

Such adhesions as existed in this case might have caused rigidity of the spinal column, but that does not appear to have been present. It seems remarkable that objective sensation was everywhere intact as late as November 29, 1900. It is possible that at that date very careful examination might have revealed some slight diminution in sensation, especially of the thorax or abdomen; it is also possible that the degeneration of the thoracic region of the spinal cord increased greatly during the last year of the patient's life, during which time no observation concerning sensation was recorded.

ON CHANGES IN THE CENTRAL NERVOUS SYSTEM IN THE NEURITIC DISORDERS OF CHRONIC ALCOHOLISM.[1]

BY SYDNEY JOHN COLE, M.A., M.D.OXON.

Senior Assistant Medical Officer, Wilts County Asylum, Devizes.

It is now well known that in alcoholic paralysis, as in other forms of toxic neuritis, the degeneration of peripheral nerve-fibres does not stand alone, but is associated with a more or less characteristic type of change in the related nerve-cells. Moreover, in recent years observations have been reported which tend to show that this combination of fibre degeneration with cell change is, at least in many acute cases of the disease, not confined to neurones which go to make up peripheral nerves, but is exhibited also by neurones of various groups situated entirely within the brain and cord. The disease is something more than a mere peripheral neuritis, and represents a very wide-spread affection of the whole nervous system. Not only does it appear to be allied to certain spinal degenerations, but it stands in intimate clinical and pathological relationship with a number of important cerebral disorders in which there may be no appreciable peripheral affection.

During three years in which I was a medical officer at Colney Hatch Asylum, there came under my observation fifteen cases of alcoholic neuritis, and in three of these I had an opportunity of making a pathological examination. The observations are here recorded. A more detailed account of case 1 will shortly appear, with illustrations, in vol. ii. of the "Archives of Neurology" of the London County

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[1] Abridged and adapted from a thesis for the Oxford M.D. degree.

Asylums. A comparative study of that case with the two others subsequently investigated, is however of sufficient interest to induce me here to give a brief abstract of it. For the three cases present not only important resemblances, but also instructive differences, so that much of their significance becomes apparent only when they are examined side by side.

The observations here recorded suggest: (1) That the peripheral and central lesions express a nervous degeneration of toxic origin, in the production of which no essential part is played by changes in interstitial tissues supporting the nervous structures, or by changes in the blood vessels concerned with their nutrition. (2) The changes in the nerve-cells are not the mere result of antecedent damage of nerve-fibres, but the changes in the fibres and cells together express a highly selective affection of whole neurones. (3) The peripheral neuritis is simply a local expression of this affection, and is not of purely local and peripheral causation. (4) The lesion of peripheral neurones is only one of many manifestations of the disease, and is accompanied by lesions identical in nature, affecting many groups of neurones situated entirely within the central nervous system. (5) The central changes are not attributable to the peripheral neuritis, and though in some cases the peripheral neurones are mainly affected, in others the morbid process chiefly implicates central neurones; but these two groups of cases do not appear to be sharply divided.

CASE 1.—*Acute alcoholic paralysis, fatal after six weeks duration, and presenting all the usual clinical and pathological evidences of acute degeneration of cranial and spinal nerves. "Polyneuritic" mental disorder. Death from vagus paralysis and heart failure. No appreciable vascular changes in nervous system. Acute cell changes in cord, spinal ganglia, medulla and cortex. Degeneration of pyramidal tracts, fronto-thalamic fibres, and the exogenous fibres of the posterior columns.*

Well-developed, well-nourished woman, aged 32, married. History of eight years' excessive gin-drinking; several attacks of delirium tremens; brief mania a potu with suicidal and homicidal impulses, July, 1898. Admitted to Colney Hatch, September 7, 1900, five weeks after sudden onset of acute multiple neuritis. Mental confusion, defective ideas as to time and place, loss of memory for recent impressions, delusion of recent confinement, and illusions as to identity of persons around her.

Complete paralysis of legs, with complete anæsthesia and analgesia, wasting of muscles and loss of reaction to faradism, and foot-drop; trophic blisters on heel and malleolus. Wasting of upper limb muscles, with marked weakness, especially of extensors; wrist-drop; diminution of faradic excitability; slight impairment of cutaneous sensation on forearms and hands without analgesia. Cutaneous sensation not perceptibly impaired on trunk, neck, and face. Weakness of muscles of neck and trunk. Partial right sixth palsy, with squint; double facial weakness, with defective articulation; tremor of lips and tongue; weakness of muscles of mastication; dysphagia; partial aphonia. General muscular tenderness to pressure, especially of limbs and abdomen; passive and active movements painful. Acute tenderness of limb nerves. Vision and hearing good; optic fundus normal; pupils reacted well to light and accommodation Knee-jerks and plantar reflexes abolished; no upper limb jerks; abdominal reflex present Partial paralysis of diaphragm. No paralysis of sphincters.

Dyspnœa and orthopnæa; respiration rate 26. Pulse 120-170, feeble, slightly irregular. Progressive cardiac dilatation, cyanosis, and hypostatic congestion of lungs. The comparatively slight paralysis of diaphragm did not appear sufficient to account for the rapid cardiac failure. No vomiting. No albuminuria. Constipation. No pigmentation of skin. No suspicion of arsenical poisoning. Patient was conscious up to the time of death, which occurred September 15, eight days after admission to asylum, or six weeks after onset of illness.

AUTOPSY.

Rigor mortis commencing. Slight excess of fluid in head. Dura mater normal. Very slight pia-arachnoid milkiness over frontal and parietal regions; no adhesion. No appreciable atrophy of convolutions. Brain 42 ozs., fairly well convoluted. No focal lesion. Basal vessels healthy. Heart 8 ozs., pale and greasy, Marchi sections showed slight fatty degeneration in places. No valvular lesion. Blood from jugulars fluid, of a dark laky colour, contained quantities of *choline*. Lungs normal, save for slight hypostatic congestion of bases. Slight fatty cirrhosis of liver. Kidneys 7 ozs. each, cortex not diminished, capsules not thickened, slightly adherent in places, slight fatty change in renal epithelium. Mucous membrane of stomach vascular and congested, with patches of chronic inflammation and fibrosis. Intestines and other organs healthy.

MICROSCOPICAL APPEARANCES.

Peripheral Nerves.—No naked-eye changes. Small cutaneous branch to heel, anterior and posterior tibials, ulnar, musculo-spiral and median, examined by Marchi's method, showed intense acute degeneration of nearly all the fibres, with multiplication of their neurilemma nuclei. Both vagi affected, nearly half the fibres giving Marchi reaction. Left phrenic contained a few degenerated fibres. Tibials showed very slight interstitial proliferation commencing in places; none in the other nerves. No vascular or inflammatory changes.

Muscles.—Thenar muscles, triceps, and diaphragm (Marchi) showed acute fatty degeneration of many fibres, with proliferation of their sheath nuclei. Transverse striation preserved. No interstitial overgrowth. Soleus showed rather less fatty change, but some impairment of striation, and a very slight interstitial increase. No naked-eye change.

Vessels of spinal cord congested, otherwise quite normal. No neuroglial, meningeal, or other non-nervous changes.

Anterior horn cells of lumbo-sacral and cervical enlargements (Nissl) show acute changes. Severe chromatolysis commencing in the centre of the cell, and thence involving the whole cell body, with slight swelling and rounding of cell, and atrophy of dendrites. Nucleus swollen, pale, and displaced to the periphery, often bulging out from the side of the cell, though sometimes flattened against it. Nucleolus and membrane stain well, and usually appear normal; the membrane, however, in a few is granular and crumpled in association with extreme nuclear displacement. Actual loss of the nucleus has been searched for in vain; but rupture seems imminent in a few. Some excess of the normal yellow pigment. Nerve cells not invaded by glia cells, or leucocytes. A considerable number of cells of the anterior median group are normal, showing abundance of large stainable masses; these cells are believed to supply the spinal muscles. But all the cells of the other groups, supplying limb muscles are affected in the manner described; none of these present even an approximately normal appearance. Those of the upper cervical and the dorsal regions are less affected than those of the lumbar and cervical enlargements. Marked changes of the same type are seen in the nuclei of the vagus, hypoglossal and sixth nerves, and the formatio reticularis, in the medulla. The cells of *Clarke's columns*, and also most of the other posterior cornual cells, are normal. The cells of the lumbo-sacral and lower cervical *posterior root ganglia* show similar lesions, very nearly one third of their number showing marked eccentricity of the nucleus, with chromatolysis.

There is degeneration of a very few fibres in the lumbo-sacral anterior and posterior roots.

Posterior columns (Marchi). Extensive degeneration of *exogenous* (posterior root) fibres, visible to naked eye in lumbar sections. No degeneration of cornu-commissural zones at any level, or of Flechsig's central oval area in the lumbar region; these situations are occupied by endogenous fibres; their integrity accords with the normal appearance of the posterior horn cells. Marked degeneration of root fibres in the root-zones, especially at limb levels. In the cervical region, there is much degeneration of the long fibres from lumbo-sacral roots, seen in the neighbourhood of the posterior median septum. Degeneration in funiculus gracilis and cuneatus.

Cerebellar tracts and *restiform bodies* not affected.

Slight degeneration in white matter of *cerebellum*, especially vermis.

Moderate degeneration of *pyramidal tracts*, through their whole extent in the cord, medulla, pons, crura, and internal capsules. In the *anterior limb of the capsule*, more degeneration than in the motor portion; numerous fibres giving Marchi reaction can be traced downwards, backwards, and inwards, into the gray matter of the thalamus.

Cerebral cortex.—Top of each ascending frontal gyrus (Nissl). Some of the Betz cells are normal; but most of them show a central and basal chromatolysis, with nuclear eccentricity, analogous to the anterior horn cell change, and of the kind described in notes of cortex of Case 2, in which the condition is more marked. Apart from slight fatty or pigmentary change, I have searched in vain for changes in the cortical blood-vessels. Marchi-Pal sections show a slight atrophy of *tangential fibres* in places. Marchi sections show a few degenerated fibres in the white matter of the motor convolutions.

CASE 2.—*Sub-acute alcoholic delirium, following fracture of femur, and fatal after ten weeks duration. Advanced fibrotic atrophy of tibial nerves. Vascular degeneration, slight in cortex, but severe in nerves, cord, medulla, and pons, with thromboses and hæmorrhages. Spinal ganglion cell changes and posterior column degeneration. Anterior cornual cell lesion. Degeneration of Clarke's cells and direct cerebellar tracts. Cortical cell lesions, and pyramidal and corticothalamic fibre degeneration.*

C. B., Italian, aged 49, female, married twenty-two years, no children. History of at least eight months excessive indulgence in white wine, brandy and gin; no beer. Had had several attacks of "nerves" (? delirium tremens). On January 26, 1901, fell downstairs while drunk, fracturing neck of left femur; no loss of consciousness. Forty-eight hours afterwards, she developed "delirium tremens," and lay in a state of constant muttering, with hallucinations, seeing cats, dogs, and other imaginary animals, and feeling them bite her; sleeplessness; refusal of solid food; constant craving for alcohol; passed urine and motions under her. Was treated in hospital and in workhouse infirmary, and from the latter was brought to Colney Hatch, on March 2.

On admission to asylum:—Poorly nourished, helpless and bed-ridden. Perpetually tossing about and throwing off the bed-clothes. No proper sleep. Much incoherent muttering. Paid no attention to questions, or to what went on around her. Once or twice recognised her husband, and asked him for brandy. Hallucinations very persistent—chiefly visual, occasionally pleasant or ludicrous. Repeatedly refused nourishment, and had to be fed by nurse. Action of bladder and bowels always involuntary. Though unable to raise herself in bed, she showed considerable power of resistance to examination; marked rigidity of arms. Elbows, wrists, and knees always flexed. Much coarse tremor of tongue, neck muscles, arms and hands. Legs almost completely paralysed. All muscles much wasted. Upper limb muscles re-acted fairly well to faradism, except triceps, which only responded to strong current. Quadriceps, calf muscles, and tibialis anticus, of both sides, scarcely re-acted to strong faradism Patient objected to strong current applied to arms, but not to legs. Cutaneous sensation could not be satisfactorily tested owing to mental state; no apparent pains or tenderness. Knee-jerks absent, plantar reflexes lively. Pupils equal, of moderate size, re-action to light sluggish. Accommodation doubtful, owing to mental state and almost complete defect of attention. Ophthalmoscopic examination unsatisfactory, owing to resistance; no obvious change in discs. Pulse 130, small, compressible, regular. Cardiac sounds weak; otherwise nothing abnormal noted in examination of chest or abdomen. Urine (by catheter) of fair quantity, clear, acid, sp. gr. 1025, albumen in readily recognisable trace. Never any vomiting, or urinous odour of breath. Temperature normal or subnormal, with occasional rise to 99° or 100°.

March 28. Small trophic blisters over right shin and left knee.

March 31. Slight diarrhœa (one day).

April 3 Absolutely "lost" and unresponsive, muttering incoherently. Coarse tremor of arms, more marked, with short series of clonic movements, of 25 vibrations in 5 seconds.

Respiration rose to 44, pulse became almost imperceptible. She lay in a moribund state several days, and died April 6, ten weeks after the accident, the delirium having persisted throughout.

AUTOPSY.

Rigor mortis present. Emaciated. Healing sores on legs. Bony union of fracture.

Calvaria and dura normal Excess of subdural and subarachnoid fluid. Slight opacity and thickening of pia-arachnoid over parietal and frontal lobes. Congestion of meningeal veins. Some rounding of convolutions and widening of sulci. Pia stripped fairly readily without tearing cortex. Cerebral vessels apparently healthy.

Lungs. Cavity in right lung, size of an olive; firm localised pleural adhesions at this spot. Some hypostatic congestion of bases.

Heart pale and flabby; left ventricle contracted and empty; whitish clot in right side and in aortic arch; slight atheroma above valves. No valvular lesion. Muscle substance from left ventricle (Marchi, hæmatoxylin) showed intense universal acute fatty change in all the fibres, but scarcely any impairment of transverse striation, and no nuclear proliferation.

Liver deformed, globular, pale; slight nodulation of under surface with thickening of capsule. Marchi and hæmatoxylin sections show a moderate fine cirrhosis of portal distribution, fairly well marked fatty infiltration, and slight fatty degeneration in liver cells; no cloudy change.

Kidneys macroscopically normal on section; very slight adhesion of capsule in places. Marchi and hæmatoxylin-eosin sections show a good deal of fatty change in the renal epithelium, especially of the medulla; slight thickening of intima and media of some of the arteries; slight interstitial overgrowth beneath capsule.

Peritoneum normal. Stomach apparently normal. Some congestion of jejunum in places; no ulceration. Spleen normal. Chronic thickening of bladder. Uterus and ovaries shrunken.

Brain weighed 40 ozs., heart 10, right lung 13, left 15, liver 36, spleen 2½, and kidneys 4 ozs. each.

MICROSCOPICAL EXAMINATION OF NERVOUS SYSTEM.

Peripheral Nerves.—Left Posterior Tibial, at ankle (Marchi, hæmatoxylin-eosin), shows very great fibrosis; the nerve bundles are almost entirely converted into dense fibrous tissue permeated by numerous small vessels. There are only a few nerve-fibres left here and there, and many of these give the Marchi reaction. There is thickening of the media and intima of many of the arteries (atheroma); some contain clots, in which focal collections of leucocytes are seen, and organisation appears to be commencing.

Left anterior tibial, in middle of leg, is in a similar condition. The anterior tibial artery shows thickening of the inner coat.

The arm nerves show much less change. Many of the fibres of the left *ulnar* (at wrist) show a cloudy granular appearance of the myelin, without segmentation; a few blackened droplets, but no definite Marchi reaction. No nuclear proliferation, or interstitial overgrowth. The ulnar artery is atheromatous, and contains a small clot commencing to organise. A large clot is also seen in a big vein lying next to it. A small artery in the nerve itself shows general thickening, and contains a clot.

Left musculo-spiral (in lower third of arm) shows slight recent degeneration. Some multiplication of neurilemmal and endoneurial nuclei, with commencing interstitial fibrosis.

Left median (at elbow) shows a few fibres giving definite Marchi reaction of degeneration. There is less nuclear proliferation than in the musculo-spiral. The median at the wrist presents the same appearances as at the elbow.

A few fibres giving the Marchi reaction are seen in the *optic nerves and tracts*.

Anterior horn cells of the cord.—These are much more affected in the lumbar enlargement than in the dorsal and cervical regions. They present the same extreme degrees of central chromatolysis and nuclear eccentricity that were seen in Case 1. At all levels, the anterior median group supplying muscles of the spine, seems to be nearly as much affected as the others. There is marked general excess of yellow pigment, which, in the lumbar cells, shows a distinct predilection for the periphery of the cell and the bases of the dendrites; in the cervical enlargement, it is more commonly seen as a mass in the midst of the cell. The chromatolysis is seen in many of the cervical cells, but not so marked as in the lumbar region; truly normal examples, however, are scarce.

Cells of posterior horns.—Nearly all these show a similar type of chromatolysis.

The same kind of change is seen in the cells of *Clarke's columns*; none of these appear normal, the great majority are entirely devoid of Nissl-bodies.

In the examination of the cells of the *posterior root ganglia*, the Nissl method was supplemented by Heidenhain's iron-hæmatoxylin. Nuclear eccentricity occurs in only a very few of them; there are no very marked chromolytic changes; there is an excess of pigment, often at the periphery of the cell. In three or four cells in each section, the nucleolus is swollen and intensely stained, while the nucleus is reduced in size, preserves its uniform oval outline, and stains somewhat deeper than normally.

Purkinje's cells of the *cerebellum* show no definite changes. There is slight fibre degeneration in the white matter of the vermis and lateral lobe.

Nissl-sections from several levels of the medulla and pons show in a number of cells of the cranial nerve nuclei, changes similar to those observed in the lumbar anterior horn cells, but more severe.

Cerebral cortex.—Upper parts of ascending frontal and parietal gyri of both sides (formol-paraffin-Nissl). None of the Betz-cells are normal. Their large masses of stainable substance are broken up into a fine powder or granular debris; the parts of the cell thus affected are distinctly paler than they should be. The alteration affects chiefly the central parts of the cell, but may extend to the periphery, in which case the basal part is more affected than the other peripheral regions. Some more or less large masses of stainable substance often persist at the sides and apex of the cell, and on the dendrites, especially the apical process. In association with a chromatolysis of this kind (which, in some few of the cells, is complete) there is observed a displacement of the nucleus to the side or to the upper extremity of the cell. The nucleus may be swollen and bulging, or may be flattened. The nucleus remains pale, its membrane and nucleolus stain with normal intensity, and the former may be granular. Many of the medium-sized pyramids are beset with glia cells. There is no disarrangement of the cell layers and columns.

Sections prepared by Busch's modification of Marchi's method show numerous degenerated fibres in the white matter of the motor convolutions, and still more in the visual area (right calcarine fissure). There is slight pigmentary change in the minute vessels of the cortex, slight thickening of smaller arteries, and some dilatation of perivascular spaces, but no perivascular infiltration. The vascular changes are trivial compared with those in the cord.

A few degenerated fibres are seen in the part of the *Corpus Callosum* opposite the motor areas.

In the *anterior limb of the Internal Capsule*, numerous degenerated fibres can be seen running downwards, backwards, and inwards, into the gray matter of the thalamus, as in the other cases.

There is considerable degeneration in the *Pyramidal Tracts*, from the internal capsule downwards to the sacral region.

The *Direct Cerebellar Tracts* and *Restiform Bodies* are extensively degenerated.

In the whole cross section of the *Posterior Columns* of the cord there is considerable diffuse degeneration, most evident in the cervical region, and diminishing as the cord is traced downwards. It is also seen in the funiculus gracilis and cuneatus in the medulla. The cornu-commissural zones have not escaped, so that the endogenous fibres appear to be implicated. But the exogenous fibres are more extensively affected; and this is more evident in the lumbar region. In the cervical part the degeneration is most marked in the posterior root fibres, in the root zones, and in Goll's columns near the middle line (situation of long fibres from lumbo-sacral roots). In the upper dorsal levels it is mostly in Goll's columns. In the mid-dorsal region it is more diffuse. At the twelfth dorsal segment it is most marked in the middle of each posterior column; there is less degeneration near the gray matter and median septum. There is not much in the lumbo-sacral region; what there is is chiefly in the root zones. Thus the lesion of the exogenous fibres (derived from posterior roots) appears to preponderate over that of the endogenous fibres.

Nearly all the blood-vessels of the cord are irregularly thickened and tortuous. There is general vascular engorgement.

There are a number of small hæmorrhages in the spinal gray matter; I have not observed any in the white columns. They occur anywhere in the anterior or posterior horn, and are most numerous in the lowest cervical segments; a few are seen in the upper dorsal region, but none lower than this. In sections stained by Van Gieson's method, there is also seen a slight increase of interstitial tissue in Goll's columns in the cervical region, and also in the crossed pyramidal tracts. Amyloid bodies are numerous in the membranes, and in the periphery of the white matter. Thrombi are seen in a few of the larger vessels of the medulla and pons.

Voluntary Muscles (Marchi, hæmatoxylin). Those of the hypothenar eminence show an acute fatty change, affecting different individual fibres selectively, and accompanied by some proliferation of the nuclei of their sheaths. There is no marked interstitial increase, and no appreciable loss of transverse striation, except in a few of the fattiest fibres. A similar condition is seen in the triceps. In the tibialis anticus, the fatty degeneration is less, there is some impairment of striation in places, and a slight interstitial overgrowth. There is thickening of the coats of the small arteries in this muscle.

CASE 3.—*Acute alcoholic mental confusion of "polyneuritic" type. Chronic neuritis. Tuberculosis of lungs. Cortical cell changes. Degeneration of fronto-thalamic fibres, pyramidal tracts, and posterior columns.*

C. K., married woman, aged 45, dressmaker; addicted to beer and spirits several years. Admitted to Colney Hatch, Sept. 8, 1900; duration of mental disorder then stated to have been one week. Short previous attack 3 years ago (not in asylum). On admission, she was emaciated and feeble, and scarcely able to stand; had been refusing her food. Depressed and apathetic; gave irrelevant answers to questions. Had no idea where she was, or how long she had been there. Often thought she was at home; talked of selling her furniture, which she thought she saw in the bare half-padded room where she lay Once she said, "This is the Hearts of Union Oak." She thought the nurse was her sister. She gave accounts of imaginary journeys she had made "yesterday" or "to-day":—she had been to church, and on her way home slipped and fell, hurting her knee; another time, she had been to Regent Street, to make designs for wall-papers (this she had never done). Thought she was required to get up and do dressmaking jobs, and protested she was unable.

Continually asking all who went near her for beer, gin or brandy; but if asked whether she liked beer she would profess disgust. Very inattentive to questions, or to what went on around. Talkative, mumbling incoherently. Constantly tossing about; had to be placed in padded room to prevent her injuring herself falling out of bed. Passed urine and motions under her.

Fine tremor of tongue, facial muscles and hands. Slight facial weakness, more on right side. All muscles of upper limbs wasted, especially triceps, interossei, and thenar and hypothenar muscles; wrist drop; faradic reaction almost abolished in deltoids, triceps, and small thumb muscles. Muscles of lower limbs flabby and wasted; marked general impairment of faradic excitability. Muscular tenderness, especially of calves, triceps and small thumb muscles. Tenderness of posterior tibial nerves. Knee-jerks absent; plantar reflexes sluggish and feeble. Cutaneous sensation could not be satisfactorily tested, owing to mental state, but there was at any rate no marked analgesia to pin-prick. Pupil reactions normal. Optic discs normal. Pulse 120, regular, feeble. Respiration 30, some cough, signs of consolidation over part of right apex. Evening rise of temperature to 100° or 101°. Became more exhausted and dyspnœic, and had several syncopal attacks, in one of which she died, six days after admission (September 13); conscious up to time of death.

AUTOPSY.

Rigor mortis present. Skull-cap and dura normal; very slight milkiness of pia-arachnoid over parietal and frontal convexity; no adhesion of membranes; no excess of fluid; practically no wasting of convolutions; brain weighed 42½ ozs.; ependyma of ventricles smooth; no focal lesions; basal vessels healthy. Small amount of caseous tubercle at apex of each lung, some hypostatic congestion of bases. Heart, 7½ ozs.; cardiac muscle pale and friable; some dilatation of right side; valves and aorta healthy. Liver, 42 ozs., soft, fatty, some passive congestion. Kidneys, 5 ozs. each, normal to naked eye; microscopically, very slight interstitial increase. Stomach, intestines, spleen, and pelvic organs, normal.

MICROSCOPICAL.

Some of the nerves were accidentally spoiled; but the posterior tibial shows a marked fibrotic atrophy, the number of nerve-fibres left being very small; some of these give the Marchi reaction. A few fibres of the median nerve give the Marchi reaction, but otherwise the nerve appears normal.

The anterior horn cells are much less changed than in the other cases; however, there is a general diminution in size of Nissl-granules, and in a fair number of cells there is definite central chromatolysis, with more or less displacement of the nucleus; there is marked excess of pigment. Chromolytic changes are more marked in Clarke's cells. The cranial nerve-cells in the medulla and pons are severely affected with change of the same type as in Cases 1 and 2; extreme displacement of the nucleus, with flattening and crumpling of the membrane. The large cells of the reticular formation are affected in like manner. No definite changes have been made out in Purkinje's cells of the cerebellar cortex; Busch sections of the vermis show numerous degenerated fibres in the white matter; the lateral lobe shows fewer.

Busch's method shows numerous degenerated fibres in the pyramidal system at all levels, in the internal capsule, crura, pons, medulla, and cord; the last was examined at nine different levels. In the anterior limb of the capsule, there are large numbers of degenerated fibres seen running backwards into the thalamus. There is some degeneration of the direct cerebellar tracts.

Of all the columns of the cord, the posterior columns show the most degeneration. In the cervical region it is most marked in Goll's columns bordering each side of the median line, and also in the root zones; there is a slight diffuse degeneration in Burdach's column; the cornu commissural zones appear to be free. In the dorsal region the degeneration is somewhat diffuse, but is most marked in Goll's columns and in the more posterior parts. In the lumbar region the central oval area of Flechsig escapes, though all around it there is a good deal of degeneration; there is marked degeneration in the posterior root zones, of fibres which have just entered the cord; the cornu-commissural zones are apparently free from degeneration. The lesion is, therefore, mainly an affection of exogenous fibres, as in Cases 1 and 2.

There are no appreciable vascular changes in the brain and cord.

The appearance of the cortex of the paracentral lobule of each side is scarcely distinguishable from that seen in Case 2. There is the same type of Betz-cell change as in the other two cases; none of these giants are normal. There is some excess of satellites about the pyramidal cells, and a slight proliferation of glia nuclei in the deeper layers. There is scarcely any abnormality in the small vessels, and no cell proliferation in their sheaths.

The cardiac muscle shows a distinct nuclear proliferation in the interstices between the fibres.

The diagnosis of neuritis in these cases is established by the microscopical appearances. All three patients were alcoholics. The form of mental disorder in each case is consistent with the view that it and the neuritis were related to the alcoholic condition. Case 1 is an example of an acute polyneuritis of cranial and spinal nerves; in the other two there is found a more chronic form. In the first case there is practically no interstitial or vascular change anywhere in the nervous system; in the third also there is very little. But in the second, vascular changes are severe in the nerves, cord and medulla, and slight in the cerebrum. In Cases 2 and 3, there is advanced fibrotic atrophy of some of the nerves The table here given may be helpful in presenting concisely the degree and distribution of the various changes. A minus sign signifies "normal," or "no appreciable alteration"; one or more plus signs indicate the presence and degree of change.

	Case 1.	Case 2.	Case 3.
Acute degeneration in nerves	++++	—	—
Fibrosis of tibials	—	++++	++++
Vascular changes in nerves	—	++++	+
,, ,, cord	—	++++	—
Anterior cornual cells:			
Lumbo-sacral	++++	+++	++
Dorsal	++	++	+
Cervical	++++	++	+
Spinal ganglion cells	++++	+	(not examined)
Exogenous fibres of posterior columns:			
Lumbar	++++	++	+
Dorsal	++	++	+
Cervical	+++	+++	+
Posterior horn cells	—	++	—
Endogenous fibres of post. columns:			
Lumbar	—	+	—
Dorsal	—	++	—
Cervical	—	++	—
Cells of Clarke's columns	—	++++	+
Direct cerebellar tracts	—	++++	+
Cells of cranial nerves	++++	+++	+++
Betz cells of cortex	+++	++++	++++
Pyramidal tracts	++	+++	+
Fronto-thalamic fibres	++++	+++	++++

We may proceed to consider the significance of the changes in the brain and cord, in relation to the general nature of alcoholic paralysis, and in relation to the peripheral neuritis. The whole question is conveniently approached by some preliminary consideration of certain features of the peripheral nerve lesions which have an important bearing on the interpretation of the central changes.

Few pathologists now hold that alcoholic neuritis consists in an inflammatory affection of the nerves. It is essentially a degeneration of the nerve-fibres, as is evident from the study of acute cases, like Case 1, or those reported by H. H. Tooth and by Sidney Martin. In such cases, the appearances resemble those seen in early stages of Wallerian degeneration after nerve section. There is severe acute degeneration of the fibres, in spite of complete (or almost complete) absence of change in the sheaths, connective tissue and vessels. Indeed, the more severe the degeneration, the more striking is the absence of vascular and interstitial changes. These cannot, therefore, be the cause of the fibre degeneration; in those cases in which such changes occur, we must regard them as secondary. For proliferation of neurilemma nuclei and connective tissue-cells, diapedesis of leucocytes, and formation of new fibrous tissue, all appear successively in Wallerian degeneration, and follow as the result of the injury to the nerve-fibres. We may therefore justifiably infer an analogous causation for the similar interstitial changes in sub-acute and chronic neuritis. So far simply as the nerves alone are concerned, the fibre degeneration is the primary element of the neuritic process.

Vascular and interstitial causes of the degeneration being excluded, at least in many acute cases, we might be tempted to ascribe it simply to direct local toxic action on the nerve fibres themselves. But the selective nature of the process is not easily explained as a selection of fibres as such. Apart from the apparent histological similarity of all peripheral fibres, we find that in the various forms of toxic neuritis certain groups of fibres are selected by one poison, and others by another. The selection therefore, cannot be due to local and anatomical factors, since they would be more or less the same for all forms. Though alcoholic neuritis is usually of the "multiple" variety, yet some nerves are affected more than others. Thus, the motor and sensory paralysis is more marked in the limbs than in the trunk, and more marked in most cases in the distal parts of the limbs than in the proximal parts This is not adequately explained as the mere result of defective circulation in the extremities, impairing the nutrition of their nerves and so rendering them more vulnerable. Nor is the marked affection of the long nerves, such as the limb nerves, phrenics and vagi, adequately explained by the fact that their fibres have a greater extent of surface exposed to toxines in the blood. For it is not universally true that the longest fibres are the most affected. Thus, one occasionally meets with cases in which the arms are more affected than the legs, or in which the deltoids and glutei are the most affected muscles, as in a case I have in Colney Hatch, which was referred to by Dr. Mott, in his Croonian Lectures. And, in quite analogous fashion, I have more than once found the sensory affection of the extremities less marked distally than proximally, sensation being less impaired on the feet than on the legs.

Moreover, the extensor muscles of the limbs are usually more paralysed than the flexors. This fact cannot be explained by blood stagnation or the length of nerves; nor can it be attributed to stress. The extensors of the legs are perhaps more used than the flexors, as in maintaining the erect posture and in walking. But in the upper extremities the reverse condition holds, for most persons use the flexors of the arms more than the extensors, and the biceps distinctly more than the triceps. Strain, or overwork of certain muscles, may modify distribution of paralysis in certain individuals of special occupations, but cannot account for the typical selective distribution in ordinary cases.

The essential feature of the muscle change is a fatty degeneration, affecting individual fibres somewhat selectively, and independent of interstitial fibrosis. The cross striation is usually unimpaired by the fatty change. The interstitial fibrosis, commonly described as the characteristic muscle change in neuritis, appears to be simply an end-product. The fatty change has not received sufficient recognition. It seems probable that the muscle degeneration is partly the result of direct toxic action on the muscle substance, and not simply of damage to the nerve supply. If so, the difference of degree of paralysis of extensor and flexor muscles may be partly determined by the physiological differences normally existing between their respective contractile tissues—differences such as those illustrated by Bierfreund's experiments. In whatever way the muscle degeneration is brought about, the limb nerves may suffer more severely than they otherwise would, because they lie in great part of their course in the midst of a large mass of degenerating muscle, and hence are bathed in lymph loaded with deleterious products; the nerves and muscles may thus to some extent be involved in a vicious circle.

But none of the various anatomical and physiological factors I have indicated can fully account for the distribution of any form of toxic neuritis. The distribution varies in type according to the particular poison or toxine at work. There is obviously a far more important principle of selection, of a very special kind, consisting in a particular preference of the individual poison for particular groups of nerve elements Only in this way can we explain the various localised forms of lead palsy, or the ocular and vagus paralyses in diphtheria Apart from neuritis, the acute intoxications afford many instances of the characteristic selection of different nervous structures by different poisons. The phenomena of idiosyncrasy show that the selection is characteristic, not only for the individual poison, but also for the individual patient. Susceptibility varies largely according to hereditary and developmental factors, and also according to acquired characters, as is shown in the establishment of tolerance and in other ways.

Such differences of susceptibility can only depend on inherent qualities of the nervous elements. We can scarcely imagine, however, that certain nerve-fibres are picked out by a particular poison on account of any qualities they may possess as mere fibres. For example, we cannot well suppose that lead selects the *fibres* supplying a particular complex group of muscles, and avoids fibres in the immediate neighbourhood going to other muscles or to the skin; for they are all so similar and similarly situated. The neurone theory, however, affords an intelligible explanation. All the fibres are exposed to the action of the poison or toxine; but particular fibres succumb to it, because their axis cylinders are simply parts of specially susceptible *neurones*, which are subjected, over the whole extent of their cell-bodies and processes, to the all-pervading influence of the poison in the blood. The peculiarities which constitute the basis for special selection by poisons must surely belong to the individuality of the neurone as a whole.[1]

If there should appear to be a selection of the long fibres, it would readily resolve itself into a selection of neurones. For the longer the fibre the more should we expect the trophic influence of the poisoned cell to become inadequate for the maintenance of the remotest parts. If there were simply a selection of fibres as such, we should expect to find more degeneration in the roots and highest parts of the nerves than there is; usually there is little or none. But on the theory of a neuronal affection the facts are explicable: as the poisoned neurone is progressively damaged, the parts which suffer most are those furthest removed from the trophic influence of the cell.

Though local conditions may have an influence (as in diphtheritic paralysis of the palate), yet in all forms of toxic neuritis the distribution forcibly suggests a selective affection of whole neurones. The changes in the brain and cord further support this view. We may pass on to consider, in relation to this question, the changes in the nerve-cells.

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[1] It has been thought by some that the validity of the neurone theory, as applied to peripheral nerves, is impugned by the observations of Vulpian, R. Kennedy, and others, on regeneration of nerve-fibres. They have shown that in the distal portion of a divided nerve, though still separated from its central connections, new fibres are developed from the sheaths of the old ones. The question thus arises, whether the peripheral axis cylinder is indeed a part of the spinal cell, as we have been wont to believe. But, at any rate, the fibre and cell are intimately associated both structurally and functionally, and injury to either reacts upon the other. Without committing ourselves on this question, we may yet conveniently retain the word "neurone" as a descriptive term, to embrace the nerve-cell and its processes, with the peripheral fibre in its whole length. For the purpose of the present argument I may, without prejudice, use the word in this sense. The different parts of such a neurone may possess a limited local autonomy, but the cell is paramount, and the whole neurone comports itself for the most part as an individual.

The changes in the anterior horn cells have been described by Achard and Soupault, Ballet and Dutil, Dejerine and Thomas, Soukhanoff, Marinesco, Heilbronner, Larkin and Jelliffe, Mott, Wright and Orange. They are well exemplified in my cases. An analogous lesion is seen in the spinal ganglion cells of Case 1 (*cf.* Soukhanoff: Wright and Orange); and a change of the same type affects the Betz cells of the cortex in each case, and also many groups of cells in the pons and medulla. In all these different situations the cell changes conform to the same type. The Nissl-bodies, or large masses of stainable substance, are broken up and reduced to a fine dust, more or less uniformly distributed in the affected parts of the cell, which thus appear faintly and diffusely stained in Nissl-sections. The process of disintegration begins in the middle of the cell, near the nucleus, and thence spreads outwards in every direction, involving the whole cell-body progressively. The last stainable masses to disappear are those on the roots of the dendrites and a few attenuated clumps around the margin of the cell. Simultaneously with this process there occurs a displacement of the nucleus to the periphery.

This form of alteration closely resembles that which section of a nerve trunk produces in the cells of origin of the nerve. It has been called "reaction at a distance," "secondary cell change," or "axonal reaction." Marinesco and others, arguing by analogy, interpret the cell alteration in neuritis as a secondary change set up by the damage to the axis cylinder in the neuritic process.

The objection to this interpretation is, that the cell change in question does not necessarily signify preceding damage to the axon.

For numerous observations show that the same change may occur under conditions in which there is no axis cylinder lesion to produce it. Thus it is seen in the motor cells of the cord (and also in Clarke's cells) after section of posterior roots (Warrington). It is found widely distributed in the nervous system in certain acute diseases, when there are no recognisable axis cylinder lesions, and when the rapidly fatal result renders it improbable that the cells have been so affected. I may refer to the observations of Ewing and Bonhoeffer on delirium tremens, of Colucci and Worcester on Landry's paralysis, and of C. Bolton on the cells of the vagus nucleus in acute fatal diphtheria. The occurrence of this cell change in acute disease of any kind is very significant, and in none more so than in Landry's paralysis. The pathology of this affection is little understood ; but whether it be a separate entity, or only a rapid form of polyneuritis, the significance of the observation is the same. The virulent character of the disease, its strong motor bias, and the appearance of its cell lesions before appreciable fibre degeneration (Worcester) speak strongly against a peripheral initiation. If, however, the disease is identical with polyneuritis, as the researches of Ross and Bury appear to indicate, then their differences become simply differences of degree, and further ground is afforded for the belief that "polyneuritis" depends upon an affection of whole neurones.

The so-called "axonal" type differs from the peripheral chromatolysis seen in the primary lesions of the cell in many acute poisonings, or after artificial elevation of body-temperature, or ligature of the aorta. But such overwhelming experimental injury can scarcely represent the appearances in all the morbid conditions in which the cell is directly affected. It would appear futile to attempt to draw a hard and fast line between primary and secondary affections of the cell ; for the neurone being a living organism, there must be a process of interaction constantly going on between all its parts.

Many poisons and toxines, which, if present in a large dose, cause a rapidly fatal result, with a "primary" type of cell change, may, on the other hand, if absorbed in smaller quantities over a sufficient period, apparently set up a neuritis, with a "secondary" type of cell change. But in each case the toxic substance is everywhere distributed in the blood, and is brought to every part of the neurone. It would seem that repeated small doses partially impair the vitality of the whole neurone, leading first to decay of its remotest parts, which then reacts on the cell and so introduces a "secondary" element into the cell affection.

But between the two extreme types, there may be any number of intermediate grades, varying according to acuteness or chronicity of intoxication, or according to differences of resistance of the various portions of the neurone. Though the nerve degeneration in neuritis probably reacts deleteriously on the cells, the changes in the neurones do not begin in their processes. This appears to be clearly demonstrated by the appearances in the sensory neurones.

The spinal ganglion cells show changes of similar type to those in the anterior cornual cells; they are especially severe and conspicuous in the acute Case 1. In addition, there is extensive acute degeneration of their central prolongations in the posterior columns of the cord. In the acute case, the posterior column degeneration appears to affect exclusively the *exogenous* fibres, which enter from the posterior roots, and which, therefore, are processes of spinal ganglion cells. The degeneration is especially severe in those exogenous fibres which are processes of cells in the lower cervical and the lumbo-sacral ganglia, corresponding to the upper and lower extremities respectively. In this case, the posterior column degeneration does not affect the endogenous fibres, or processes of cells in the gray matter of the cord, such fibres are mainly situated in the cornu-commissural zones, and, in the lumbar region, in Flechsig's central oval area. These are normal.

The conspicuously selective affection of the exogenous fibres, especially those from arm and leg roots, clearly shows that the cord lesion represents a degeneration of those same sensory neurones whose peripheral processes are degenerated in the nerves, and whose cells show changes in the corresponding root ganglia. At the same time, very few of their root fibres outside the cord give the Marchi reaction of degeneration; the parts nearest the trophic cells are the least affected.

The view which accords best with these appearances is that which regards the central and peripheral fibre degenerations as simultaneous manifestations of a single disorder of the whole sensory neurone. And, indeed, no other explanation seems admissible. For what conceivable alternatives have we?

I am not aware that it has even been suggested that the neuritis is secondary to the posterior column degeneration. Such a theory would not only lack evidence, but would appear to be negatived by the fact that section of posterior roots does not produce nerve degeneration. It is equally easy to dispose of the converse theory—that the cord lesion is originated by the nerve lesion. For after section of a nerve, or amputation of a limb, the Marchi method shows no degeneration in the posterior columns; there is only a very slow disuse atrophy. Thus the lesions of central and peripheral prolongations cannot stand to one another in any way in the relation of cause and effect, unless we at the same time postulate an impairment of the resistance of the whole neurone; in other words, a general affection of the neurone.

The only remaining alternative is that the cord lesion is a phenomenon entirely independent of the neuritis. But this would require us to believe that even in uncomplicated typical acute cases, the sensory neurones are damaged by two simultaneous processes, both of which, though quite distinct from one another, yet, by some curious coincidence, have a notable selective preference for the same group of neurones, and even for its particular sub-groups (those of the limbs). This is Heilbronner's view, though he gives no valid reason for such a disregard of the logical injunction against multiplication of causes. He bases his contention mainly on the appearances in the root fibres in his Marchi preparations. Those of the anterior as well as the posterior roots appeared to be degenerated within the cord, but not outside; the change was sharply marked off at the point where they entered or issued from the cord. He therefore thinks that the affection of root fibres within the cord is a separate lesion, *sui generis*. He admits that it cannot be attributed to a meningeal lesion at the point of entrance or exit; for, on the Wallerian principle, that would cause the anterior root fibres to degenerate outside the cord, away from their cells. Moreover, there is no evidence of such lesion. The crux of the matter lies in the paradoxical appearances in these motor fibres, which gave the Marchi reaction of degeneration in the nerves and within the cord, but were normal in their intermediate parts situated in the roots. That their intermediate portions could remain normal under such circumstances seems incomprehensible, and quite at variance with all we know of their behaviour.

There would appear to be some fallacy in the observation. Heilbronner seems to realise this to some extent, and considers several possible fallacies ; but he overlooks the most probable, which is, that the anterior root fibres in the cord were not really degenerated, but gave the Marchi reaction because of *post-mortem* damage. If the roots are pulled upon in removing the cord from the body, the root fibres outside the cord are protected by their tough external sheath ; but their continuations within the cord have no such protection against stretching, and hence their myelin is damaged. Blackening in Marchi specimens under such circumstances is a familiar observation, and of no pathological import.

But that the degeneration of exogenous fibres is genuine is shown by its systematic distribution over the cross section of the posterior columns at different levels, the long lumbar fibres being degenerated even in the cervical region. Damage by stretching could only extend a short distance into the cord. Thus we can be sure that there is real degeneration of these fibres. But outside the cord they may be better able to preserve their myelin, as there they have primitive sheaths, and are nearer their cells.

By such a process of exclusion of alternatives we are reduced to our first hypothesis, viz., that of a general affection of the whole sensory neurone.

Moreover, the degeneration must begin in the neurone itself, for in many of the severest cases there is no meningeal, interstitial, or vascular change. Yet I would not be thought to undervalue the importance of vascular lesions. In Case 2 there is advanced vascular degeneration, and in the spinal cord there are numerous small hæmorrhages. Such lesions must inevitably cause damage of the nervous elements. But the exogenous degeneration is more conspicuously selective, and even more intense, in the acute case without vascular lesions, than in the case with vascular lesions. There is, therefore, a selection of these neurones, independent of alteration in their structural environment.

The theory of a general affection of whole neurones is especially supported by severe acute cases, like Case 1; but in the less virulent cases, more opportunity is afforded for the modifying influence of differences in the constitution and environment of the two prolongations of the sensory neurone. They are probably not homologous, and in the peripheral process conduction of impulses is cellulipetal, while in the central it is cellulifugal. There is a more liberal blood-supply in the nerves than in the posterior columns; but blood stagnation in the extremities may render the peripheral process more vulnerable to toxic action, and it seems also more liable to poisoning by products of muscle degeneration. On the other hand, in some cases, the central process is more liable to damage from vascular lesions. The peripheral fibre has a primitive sheath, but the central has not; for this and other reasons, the central fibre has less capacity for repair, if its axon be broken. Waste substances are probably more rapidly removed from the nerves than from the cord; this is, at any rate, true of the products of myelin degeneration which give the Marchi reaction; hence allowance must be made for this fact, in the interpretation of Marchi preparations. And just as clinical experience shows that the neuritic condition admits of improvement, so the microscopical appearances in the nerve-cells and spinal roots show that the affection usually stops short of destruction of the neurone. Therefore, if the axon of either prolongation be only partially impaired, or be able to grow again, its myelin may be restored. In long-standing cases, the appearances may be modified by all these multifarious circumstances, especially if amelioration has taken place. But in acute cases, like Case 1, the morbid process reveals itself as a general affection of the whole neurone. Hence we find a more or less equal degeneration of the central and peripheral prolongations simultaneously, and also a cell change.

The fibre degeneration may perhaps be likened to gangrene of extremities arising in an old man as the result of general impairment of vitality. As this impairment may lead to a symmetrical gangrene of both feet, so the affection of the whole neurone may lead to degeneration of both its prolongations. But just as the gangrene does not necessarily involve the whole limb, so the proximal parts of the neurone may escape actual degeneration; though, as the proximal parts of the affected limb may be in a state of low vitality without actually becoming gangrenous, so it is possible that the myelin of those parts of the fibre nearest the trophic cell may be altered, though not to such an extent as to give the chemical test on which the Marchi reaction depends. Just as the gangrene further impairs the patient's originally feeble state, so the degeneration of the outlying parts of the neurone reacts upon the cell. Moreover in the same way that external injury may determine gangrene in a feeble patient, so unfavourable local conditions may precipitate the onset of degeneration in an already impaired neurone. Also as slight injury may determine gangrene in one or other foot, so any slight unfavourable difference of environment may determine degeneration in one or other prolongation, central or peripheral; so that in some cases (*cf.* Vierordt) the central prolongation of these neurones may be chiefly affected, and in others (*cf.* Marinesco) the peripheral prolongations. But in the same way that the gangrene would not have occurred in a healthy patient, so the fibre degeneration would not have occurred in a healthy neurone. To suppose that the fibre degeneration is the cause of the neurone affection, would be analogous to supposing that gangrene is the cause of senility. Just as many old men present the conditions favourable to the production of gangrene without actually developing it, so, too, many neurones show the characteristic cell change without fibre degeneration; this is seen in many of the cortical neurones (*e.g.* in Case 3). The analogy must not be pushed too far, however, for under appropriate conditions the degenerated fibre may be restored, though a gangrenous limb can never grow again. Also, I would not be thought to imply that the toxic neuronal affection is actually a premature senility, though the marked excess of pigment in many cells resembles that seen in old age.

Posterior column degenerations in polyneuritis have been described by Vierordt, Korsakow, Kojewnikow, Pal, Biedekarken, Campbell, Soukhanoff, Heilbronner, Wright and Orange, Goldscheider and Moxter, and Marinesco. It seems usual for such lesions to be present; for I can find no record of any case in which the cord was examined by Marchi's method, in which it is stated that the posterior columns were free from degeneration. In Marinesco's case, there was degeneration mainly of endogenous fibres; but with this one exception, an analysis of all the above records shows that the degeneration affected chiefly the exogenous fibres, belonging to peripheral neurones. In my Case 1, the degeneration appears to affect the exogenous fibres exclusively. In Case 2, both systems are affected, but mainly the exogenous. In both cases, the fibres most affected are those derived from the roots connected with the arm and leg. In Case 3, the degeneration is slighter, mainly exogenous.

The occasional affection of the *endogenous* tracts of the cord is not surprising, as the disease evidently affects neurones of many different orders. In Case 2, the lesions of posterior cornual cells and the endogenous fibres in the posterior columns, and the lesions of Clarke's cells and the direct cerebellar tracts, may be partly due to vascular damage. In the light of Warrington's experiments, however, (*vide supra*), one might be tempted perhaps to explain them on van Gehuchten's principle of the reaction of the ganglion cells of a nervous chain upon one another; the secondary spinal afferent neurones might be thus affected because their peripheral stimuli are cut off by reason of the neuritis. But if so, the absence of changes in these secondary neurones in Case 1 is remarkable, unless their development was forestalled by the patient's early death. I am strongly inclined to think that their absence here, and their marked preponderance in

Marinesco's case, point rather to a primary element in the endogenous degenerations, determined by a special susceptibility of these neurones in certain patients.

The affection of the exogenous fibres commonly makes the posterior column degeneration approximate in distribution to that of tabes. This reminds us that cases of alcoholic paralysis have been described, in which ataxic symptoms have been prominent, sometimes overshadowing the neuritic symptoms proper. For such cases, the name "alcoholic pseudo-tabes" has been devised. It is not impossible that in rare instances there may be a difficulty of diagnosis. We may bear in mind that neuritis is typically associated with posterior column degeneration of more or less tabetic distribution, that neuritis may not be conspicuous in its late stages, and also that in true tabes there is often some neuritis as well. Argyll Robertson pupil, however, may probably be regarded as unknown in neuritis, apart from previous syphilis. It was not met with in twenty-eight cases of alcoholic neuritis in which I examined the pupils; nor did any of these exhibit the reverse condition, which Lauder Brunton describes as characteristic of alcoholic neuritis, viz., abolition of contraction to accommodation, with preservation of the light reflex. I might point out, however, that there is very often considerable difficulty in inducing the patient to accommodate for near vision, owing to the defect of attention, which is part of the disease; I have always found that when the patient can be persuaded to accommodate, the pupil contracts normally, except in cases where there is general sluggishness and limitation of all pupillary movements. The pupil condition in most of my cases was normal, confirming the usual description of the text-books. But I have occasionally met with a general sluggishness such as I have alluded to: in one case, the pupils were almost fixed for some weeks, yet recovered perfect movement as the neuritis improved; in this case, the associated mental confusion was profound.

The fact that mental disorder of some sort is almost invariably present in alcoholic polyneuritic cases is evidently of pathological significance, as showing that cortical neurones are affected. One cannot too strongly insist that this mental disorder is an important part of the disease. Its prominent feature is, in most cases, a pronounced mental confusion, with disorder of observation, and failure of capacity for retaining recent impressions. Hence arises a defect of orientation as to time and place, and loss of memory for recent events, often with illusions as to the identity of persons. The "romancing," illustrated by the pseudo-reminiscences of imaginary journeys, depends probably upon this defect. The disorder was well exemplified in Cases 1 and 3.

The late Prof. Korsakow, of Moscow, showed that the same "polyneuritic psychosis" might occur in neuritis from any toxic cause, though there can be no doubt that alcohol is incomparably the most frequent. During the last three years, I have had under my observation at Colney Hatch fourteen cases of alcoholic neuritis, all with more or less characteristic disorder, without counting Case 2, in which there was a "delirium." And of fourteen other cases which I examined in Poor-Law Infirmaries, all presented marked confusion, and might equally well have been certified as insane. Certification, however, seems to be determined largely by collateral circumstances, such as the number of available beds, or the question whether the patient is in any way troublesome, or is physically fit to be removed to an asylum. The cases met with in the asylum do not differ in any essential respect from those seen outside. But, in both groups, though the defect of attention, memory and orientation is seldom wanting, other features are variable.

The mental disorder is doubtless related in some way to the cortical changes. The striking feature in each of my cases is that the Betz-cells and other large pyramids show the very same type of change as that seen in the anterior cornual cells. With this, there is diffuse, bilaterally symmetrical degeneration of many of their related fibres in the pyramidal tracts. Horizontal sections of the internal capsule show (in addition to degenerated pyramidal fibres) very numerous degenerated fibres in the anterior limb, which disappear in the gray matter of the thalamus; these apparently connect the thalamus with the motor and frontal cortex, but I have not been able to decide whether they belong to cortical or to thalamic cells. The tangential fibres of the upper motor region were examined in Case 1, and showed a slight degenerative atrophy, as in Jolly's cases.

The combination of this so-called "axonal" cell change with fibre degeneration in the cortical neurones is identical with that seen in the peripheral neurones. Thus, alcoholic neuritis is not peripheral merely, for its characteristic lesion is equally marked in higher neurones which are entirely central. Meyer found a similar condition in eight cases of "delirious and depressive disorders," and speaks of it as "central neuritis." As in his cases, so in mine, the changes in the cortical vessels and neuroglia are very slight, and seem quite insufficient to account for the cell changes. As in his cases also, focal production of the fibre lesions can be excluded absolutely in Cases 1 and 3, and with extreme probability in Case 2. There is clearly a selective affection of neurones. In Cases 2 and 3, the more acute "central neuritis" appears to be superimposed upon an older peripheral neuritis. In Case 1 both are seen in the acute stage together.

Reports of the occurrence of this Betz-cell change (with or without mention of pyramidal tract degeneration) in cases of polyneuritis, appear to be limited to two cases by Faure,[1] one by Turner, and one by Wright and Orange; that it was present in Wright and Orange's case is shown by their diagram rather than by their not very lucid description. To these I would now add my three cases. It seems likely that this cortical change may be common, or usual, in alcoholic neuritis; it has apparently been seldom looked for, as descriptions of cortical cells in this disease are extremely few. The point of interest is that the lesion of cortical neurones is now brought into line with that of peripheral neurones.

The special form of Betz-cell change seen in these examples is not confined, however, to cases of definite and pronounced peripheral neuritis, but is also found in other alcoholic, delirious and confusional disorders.

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[1] These appear to be the same two cases as those reported by Ballet and Faure.

Cases which present, on the clinical side, some form of psychosis, and on the pathological side, an "axonal" Betz-cell change or "central neuritis," appear to group themselves under the following heads:—"Polyneuritic psychosis," with or without recognised peripheral neuritis (Faure, Wright and Orange, Turner), delirium tremens (Ewing, Bonhœffer), various sub-acute delirious conditions (Meyer), confusional states, often with depression (Meyer, Turner, Cauria), and perhaps Landry's paralysis, when associated with cerebral symptoms (Worcester). This list is necessarily imperfect as a classification, for there is considerable overlapping of types. We have to do with a group of closely allied disorders, including many intermediate mixed forms.

Though we are not in a position to state that these are all pathologically identical, we can at any rate say that, in addition to this similarity of microscopical appearances, they present many interesting points of resemblance in their etiology, pathology, symptoms and physical signs. The generalisation thus dimly foreshadowed may prove to be less fantastic than it at first sight appears.

To the demonstration of the similarity of these affections as regards cortical changes, afforded by the researches of those whose names I have given in brackets, I would endeavour here to add a rough outline of some of their miscellaneous clinical resemblances.

Such experience as I have is quite in accordance with Jolly's observation, that a very close relationship exists between the polyneuritic psychosis and delirium tremens. Frequently in cases of marked neuritis there is, in addition to the confusion, a delirious condition, indistinguishable from delirium tremens, with marked tremor and jactitation, and often characteristic visual hallucinations (as in Case 2). In ordinary delirium tremens we find the same marked defect of attention, memory and orientation: Kraepelin mentions the occurrence of pseudo-reminiscences, and delusions as to the identity of persons around: and very often, as Jolly has observed, at the height of delirium tremens slight neuritic symptoms appear, such as tenderness of muscles to pressure. The neuritic psychosis is often at its onset exactly like delirium tremens, though afterwards it may pass into a condition corresponding more to Korsakow's type; and many neuritic patients whose symptoms in the daytime are mainly confusional, at night are restless and delirious, with auditory or visual hallucinations, the latter being frequently of the same type as those seen in delirium tremens (animals of various kinds, &c.); and there is often a distinct element of fright, or dread, sometimes with delusions of physical torture. It may be difficult to decide whether a given case (*e.g.*, Case 2) is a delirious neuritic psychosis, or a delirium tremens; the question indeed seems little more than a quibble.

In the polyneuritic disorder, as in delirium tremens, there is often marked defect of co-ordination and equilibration; and each of my three cases shows a degeneration in the white matter of the cerebellum, especially of the vermis, similar to that which Bonhœffer found in delirium tremens. As also in some of the cases of delirium tremens which Bonhœffer has described, so, in the neuritic cases, one not infrequently observes symptoms suggestive of focal lesion of particular cortical areas, yet without any macroscopic meningeal or vascular change. These symptoms, though severe at the time, often pass off so rapidly and completely, that the diagnosis of gross lesion is soon shown to be erroneous. Thus, in the second week of my Case 1, there was a condition of coma with hemiplegia, corresponding to which the pathological examination revealed nothing. Coma was complete for forty-eight hours; the hemiplegia gradually passed off in the course of the next eight days. In Case 2, one might perhaps at times have been inclined to suspect some lesion of the visual area; if one made a feint to strike the patient, there was not even a reflex closure of the lids, though her eyes were wide open, and she was talking at the time; the head and eyes were nearly always turned towards the left, especially when the visual hallucinations were active. As in delirium tremens, irregular jactitation, and also rhythmical convulsive clonic jerking of the limbs, of a somewhat significantly epileptiform type, are frequently observed in polyneuritic cases, as in Cases 1 and 2, and, to a less extent, in 3. These irritation-phenomena are doubtless of cortical origin.

There is an overlapping of types, not only between delirium tremens and the neuritic psychosis, but also between each of these and the other disorders I have mentioned.

Alteration of the reflexes is common in all, but varies according as the cortical or the peripheral lesions predominate; if the former, then rigidity of the limbs may also be observed.

Meyer thus sums up the clinical features in his eight cases of "central neuritis": "After a course in which there is no suspicion of organic disorder, there appears, more or less suddenly, difficulty of locomotion, increasing weakness for co-ordinated movements, at times jactitations of the limbs, and rigidity, and disorders of the reflexes, often together with diarrhœa and occasional febrile fluctuations; the mental condition is either that of anxious perplexed agitation, delirium, or stupor, similar to a protracted delirium tremens." There was evident defect of orientation in his Cases 2, 3, 5, 7, 8, doubtful in Case 1, and none was made out in Cases 4 and 6. An alcoholic history was present in Cases 5 and 8, denied in Case 7, while as to the others there is no statement. There was a history of lead-poisoning in Cases 4 and 6, which is somewhat significant in view of the well-known tendency of lead to induce neuritis. Many features of Meyer's cases suggest some form of toxæmia.

It is interesting to compare my Case 2 with these examples. The patient, as the result of a fracture, developed within a few hours what appeared to be a delirium tremens, with the usual tremor, excitement, and tactile and visual hallucinations of cats, dogs, &c. But instead of terminating in the usual way, in rapid recovery or death, the condition was protracted for ten weeks, and there were observed the same rigidity of the arms, obstinate refusal of food, and slight diarrhœa before death, as were presented by

Meyer's cases; while, in addition, there was polyneuritis, and the spontaneous clonic movements of the limbs so frequently seen in polyneuritic conditions.

In all these various disorders—delirium tremens, neuritic psychosis, confusional insanity, &c.—in addition to the defect of memory and orientation, the pseudo-reminiscences, visual hallucinations, excitement, tremor, speech disorder, jactitation, rigidity, alteration of the reflexes, and so forth, there may be also hallucinations of threatening voices, delusions that food is poisoned, obstinate refusal of food (as in my Cases 2 and 3), and delusions of physical persecution and torture. In all these conditions there is frequently also marked depression, almost deserving the name of melancholia.

It may be observed in passing that in Korsakow's type of neuritic psychosis, the melancholic factor is sometimes incidentally illustrated in a curious way by the romancing. I have several times noticed that the imaginary journeys have been either fruitless, or attended by some mishap, such as a fall (*cf.* Case 3) or sudden illness, or a fright from a runaway horse; or the patient tells us that she found her mother very ill; or she sends her little girl to fetch the supper beer, but the child drops the jug as she is bringing it home. The pseudo-reminiscence of these imaginary misfortunes is the occasion for tears.

With regard to confusional insanity, it may be pointed out that Korsakow's "polyneuritic psychosis" is really a marked form of confusional disorder. Meyer's "delirious and depressive" cases are closely allied, not only to delirium tremens, but also to the neuritic psychosis and confusional insanity. He does not appear to have examined any of the nerves in his cases. In my experience, slight neuritis is not very uncommon in alcoholic confusional states, but it requires to be systematically looked for. In Cases 2 and 3, it was by no means obvious clinically, though there was extreme atrophy of the tibial nerves.

As to Landry's paralysis, I would simply remark that in Worcester's case there were somewhat analogous mental symptoms, and also that Ross and Bury have shown that, as regards the peripheral affection, no hard and fast line can be drawn between Landry's paralysis and polyneuritis.

Jolly's observations show that in some cases of neuritis the mental disorder may be very slight (possibly, even, altogether absent), and that, on the other hand, Korsakow's polyneuritic psychosis may occasionally occur without definite peripheral neuritis. Side by side with this may be set the pathological observation of the occurrence of this neuritic lesion of cortical neurones in certain cases apart from recognised peripheral neuritis; to Meyer's cases, and those he quotes, may now be added those of Cauria. There is no doubt that in certain patients the cortical neurones are the more vulnerable, and in others the peripheral. Our conception of neuritis must be widened, and not restricted to so-called typical cases. The selective action of the toxic agent (whatever it be) is clearly modified by differences of resistance of the various neurone systems, depending largely on hereditary and developmental factors, and the occupation and habits of the patient. Even in mere drunkenness, one man's liquor flies to his head, and another's to his legs.

We have seen that the neuritic, delirious and confusional conditions displaying this characteristic cortical change present numerous clinical resemblances. They also have much in common as regards their etiology.

Neither polyneuritis, delirium tremens, nor the confusional disorders can be regarded as the expression of a mere alcohol-poisoning. They have a more complex etiology, and present the characters of a severe general disease, of the nature of a toxæmia, depending probably on an auto-intoxication from disordered metabolism. They may, most of them, result from other poisons besides alcohol, though their appearance is evidently favoured in a very special way by chronic alcoholism. But they only result indirectly from the alcoholism, and require the co-operation of various contributory or exciting causes, such as shock, surgical injury, chill, pneumonia, tuberculosis and other febrile and afebrile illnesses, want of food, the onset of the menopause, &c.; Judson Bury mentions cases of polyneuritis following injury to the head. The patient may have been addicted for years to alcohol, but the introduction of one of these additional factors suddenly gives rise for the first time to one or other of these disorders.

Moreover, all of them, but especially neuritis and delirium tremens, present a series of features directly suggestive of an auto-toxic origin. Not only do we see that many of their contributory causes are of a kind eminently calculated to cause derangement of metabolism, but we cannot fail to note the frequent occurrence of circulatory disturbance, rapid pulse, acute fatty degeneration of the heart and skeletal muscles, pyrexia without recognisable cause, profuse paroxysmal sweats even in afebrile cases, albuminuria, and sometimes diarrhœa as the end approaches; while, at least in delirium tremens, there is an alteration of the blood-count, with increase of polynuclear leucocytes, and diminution of eosinophile cells (Elsholz). All these phenomena are strongly suggestive of a severe toxæmia; and so also, I think, are many of the nervous manifestations—such as the various sensory disturbances, the motor weakness, tremor, inco-ordination, giddiness, speech disorder, twitchings of muscles, and epileptiform convulsions. Jolly has pointed out the toxic significance of many of these, both in delirium tremens and in neuritis. They remind us of the analogous symptoms seen in acute alcohol-intoxication. Similar suggestive features are far from uncommon in many other delirious and confusional states.

The frequent chronic gastritis, and the fatty, cirrhotic, and other disorders of the liver and kidneys, may be etiologically important. Cirrhosis of the liver, however, was very slight in two of my cases, and absent in the third, supporting the generally accepted opinion that marked cirrhosis is uncommon in neuritis, and perhaps also suggesting that the toxæmia does not set up neuritis unless at the same time there is nervous instability. Beer was a factor in Case 3, but not in the other two; the cases I have seen do not support the theory that arsenic is always a factor in alcoholic neuritis, but rather suggest that spirits are an important cause. This is consistent with the auto-intoxication theory, inasmuch as it seems to add weight to the gastro-intestinal and hepatic affections. The choline present in the blood in great quantity in Case 1 is, of course, of no etiological significance; it simply indicates the great amount of myelin degeneration in progress at the time of death.

The fact that the so-called "axonal" Betz-cell change is seen in acute forms, like delirium tremens, is opposed to the view that it is secondary to an axis-cylinder affection. And in my Case 3, as in some of the cases of Meyer and Faure, though the pyramidal tract degeneration was comparatively slight, *all* the Betz-cells showed this change. In the acute cases the cell changes far outweigh the fibre degeneration; the latter appears to be simply a secondary manifestation of the disorder of the neurone. The cell changes are almost certainly primary. In some of Bonhœffer's cases the changes in many cells showed characters approaching those of Nissl's "acute alteration," which is good evidence of a primary affection. In other delirious cases clinically indistinguishable, he found a much more definite "axonal" type; his description[1] would apply accurately to the cells in my neuritic cases, and so also would Ewing's.

In all these varieties of nervous disease occuring in alcoholic patients, the affected neurones, central and peripheral, present the same essential lesion—a cell change of distinct type, with or without degeneration of the myelin sheath of the parts most remote from the cell. The changes in the neurone do not begin in the prolongations, but express a disorder which leads to such general impairment of the whole neurone, that the parts furthest from the trophic centre degenerate. The affection is polyneuronal rather than polyneuritic. In all forms, we have to do with a general toxæmia, affecting whole neurones of many different orders throughout the nervous system, and rarely or never affecting peripheral neurones only. In some cases the peripheral neurones are the more vulnerable, in others the central. Hence in some cases the "peripheral neuritis" predominates, in others the "central neuritis." Thus the physical illness is closely related to a number of affections which come within the province of the alienist. The typical case of severe peripheral neuritis, familiar in the hospital ward, is connected by any number of intermediate mixed forms, with several varieties of confusional insanity, delirium, and allied disorders, in which there may be no appreciable peripheral affection.

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[1] "Die grossen Pyramiden; der Zell-leib nicht gleichmässig tingiert; einzelne fast ganz farblose Stellen; die farbbare Substanz zeigt in einzelnen Zellen noch Reste der parallelen Anordung; namentlich in der Peripherie sind zahlreiche grabkörnige Partikelchen; die Fortsätze sind nicht abnorm lang; der Kern ist wandständig, gross, blass."

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CASE SHOWING (1) DEFECTIVE DEVELOPMENT OF DURA MATER, (2) OLD MENINGITIS, AND (3) INTERNAL HYDROCEPHALUS.

BY HARVEY BAIRD, M.B., CH.B.EDIN.

Assistant Medical Officer, West Riding Asylum, Wakefield.

AT an autopsy on the body of an idiot male, aged 40 years, the following facts were noted.

The skull-cap was thin and dense, and somewhat asymmetrical, being flattened anteriorly and to the left. Dolicocephaly was present to a considerable extent. The external surface of the dura mater appeared normal. There was no thickening nor undue adhesion. The falx cerebri was absent, except for two minute folds—one an inch in front of the olfactory bulb, the other at the level of the occipital lobes. The tentorium cerebelli was absent except a small portion on each side which projected inwards for about an inch at its widest part. A small ridge represented the falx cerebelli. The pia-arachnoid was thickened and opaque, especially over the vertex. The great longitudinal fissure was obliterated by pia-mater, the arachnoid passing uninterruptedly over it. The interval between cerebrum and cerebellum was similarly obliterated, pia-mater uniting the one to the other, except where the portions of the tentorium were present. The thickening and adhesion of the pia-arachnoid was much less marked on the base of the brain. The meningitis had been mainly lateral and vertical, especially the latter. There was considerable thickening and adhesion about the Sylvian fissures. There was a moderate amount of clear fluid in the subarachnoid space, much in the cisternæ magna and pontis. The brain mantle was wasted. The cerebrum was nearly symmetrical, the convolutions of natural arrangement.

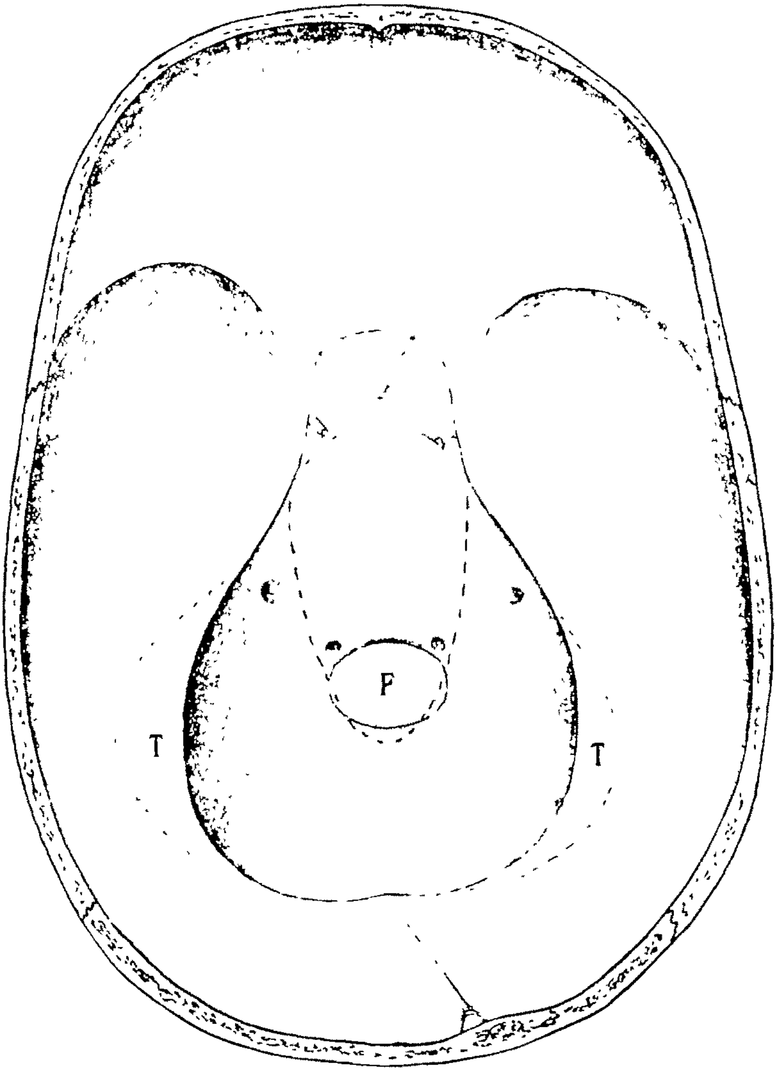

FIG. I

On making a frontal section of the brain, the interior was found to consist of one large cavity, the various ventricles having united into one. The cavity was five inches long, and three and a half inches broad. The cornua of the lateral ventricles were much dilated. The structures in the region of the fifth ventricle had entirely disappeared. The roof of the cavity was formed by white matter laterally, and centrally by a somewhat flattened corpus callosum, on the under surface of which were irregular rounded tubercles of gray matter. The floor of the cavity owing to the fusion of the third with the lateral ventricles became practically the normal floor of the third and lateral ventricles, though much more of optic thalamus and caudate nucleus was visible than usual. The posterior cornua had fused with the suprapineal recess which was much distended. The aqueduct of Sylvius was of the usual calibre.

The patient is stated to have had scarlet fever when 3 years old, and to have been imbecile ever since.

One must assume that the abnormalty of the dura was congenital. Probably the meningitis would be a complication of the scarlatina, and, owing to the absence of dura mater, one can readily understand the adhesion of cerebrum to cerebellum, and of the two lobes of the cerebrum to one another along the great longitudinal fissure. The meningitis would, of course, also cause the internal hydrocephalus by blocking the means of communication from the ventricular cavities to the subarachnoid space.

DESCRIPTION OF FIGURES.

FIG. 1.—*A view of the base of the skull showing the defective development of the tentorium cerebelli (T).*

The normal outline of the tentorium is indicated by the coarsely dotted line, while the finely dotted line indicates the situation of the lateral sinus. Posteriorily is seen the remains of the falx cerebelli as a very thin ridge displaced to one side. *F.* Foramen magnum.

FIG. 2.—*Photograph of Frontal Section of Brain through tips of Cunei.*

The pia-arachnoid fills up the great longitudinal fissure, and the greater part of the interval between the cerebrum and cerebellum, there being no falx cerebri, and the tentorium being absent except as indicated laterally.

The lateral ventricles are very considerably dilated, and have been fused into one cavity. The posterior cornua have fused with the suprapineal recess, which is also much distended.

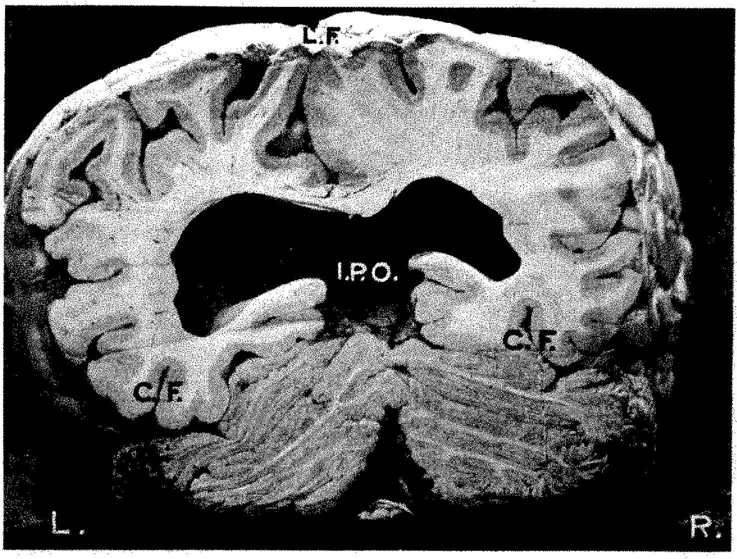

FIG. 2.

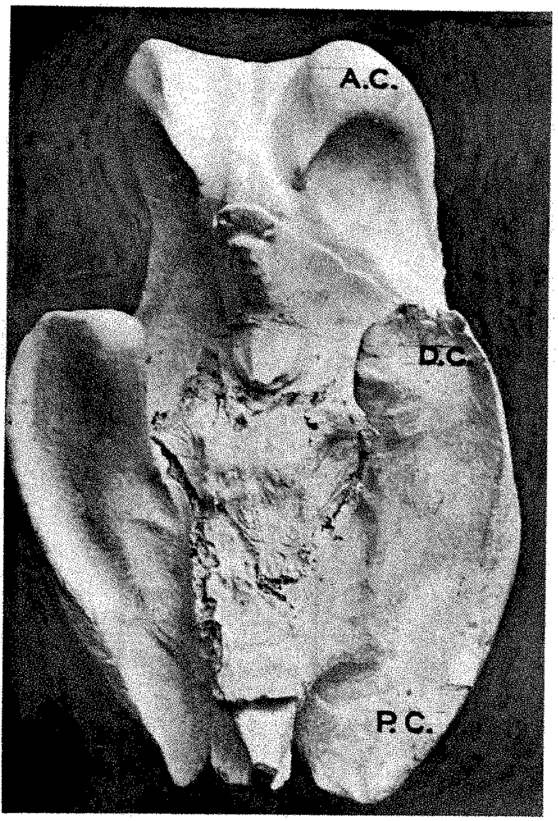

FIG. 3.

The arachnoid passes uninterruptedly over the great longitudinal fissure, which is displaced to the left and passes in a curved direction inwards.

The cerebellum is united to the cerebrum by pia-mater, except for about an inch on each side, where there is a depression into which the portion of the tentorium which is present dips.

The brain mantle of the cerebrum is much wasted.

The cerebellum is not wasted nor otherwise changed in naked-eye aspect.

FIG. 9.—*Photograph of Cast of the Fused Ventricular Cavity (under surface).*

The irregular surface in the centre is due to the vessels of the choroid plexus.

A.C. Anterior cornu.
D.C. Descending cornu.
P.C Posterior cornu.

For this cast I am indebted to Dr. J. O. Wakelin Barratt, late pathologist to the West Riding Asylum, Wakefield.

PAIN.[1]

BY JAMES MACKENZIE, M.D.

Burnley.

I.—Introduction.
II.—Definition.
III.—The pain of the digestive tract.
IV.—The pains due to gastric ulcer.
V.—Superficial and deep cutaneous hyperæsthesia.
VI.—The absence of spinal nerves from serous membranes.
VII.—Muscular hyperæsthesia.
VIII.—The viscero-muscular reflex.
IX.—The results of stimulation of exposed viscera.
X.—Testicular pain.
XI.—The mechanism by which the sensory symptoms in visceral disease arise.
XII.—Some theoretical considerations.

I.—INTRODUCTION.

I FEEL some hesitation in appearing before you with such an array of facts as I intend to present. The observations I have made have involved no deep or prolonged investigation, but are mainly the clinical symptoms that are found in the routine examination of patients. The deductions I have drawn from these symptoms are opposed to all the teaching and traditions of the profession. Though I am myself convinced of the justness of my deductions, I fear that my presentment of the reasons of the faith that is within me may not carry conviction to your minds. I trust, however, that it will cause some of you to enquire whether these things be so or not.

In the first place, might I ask you to approach this subject untrammelled by any preconceived ideas, and even to dismiss from your minds, if it be possible, the results of your own experience. My reason for this suggestion is that hitherto the consideration of the sensory symptoms have been based on an imperfect appreciation of the situation in which the symptoms were felt. Thus, for instance, a leading authority describes a tenderness of the heart muscle as a symptom of myocarditis, because he found that when he pressed his finger over the heart pain was felt. Or again, a tender liver is frequently recognised, because pain is felt when pressure is applied over the organ. In such cases the observation is unreliable, because no means are taken to ascertain the sensitiveness of the tissues between the finger and the organ. Similarly peritonitis is commonly supposed to be present when there is hardness of the abdominal wall with pain on pressure; for it is usually assumed that the pain arises from stimulation of the sensitive peritoneum, without considering that sensitive structures external to the peritoneum are being stimulated.

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[1] Read before the Neurological Society of London, October 28, 1902.

But not only have clinical observers drawn too hasty conclusions, but physiologists are not a little to blame for fostering an erroneous view in regard to the functions of certain of the sympathetic nerves. One frequently meets in physiogical writings the bald statement that certain nerves in the sympathetic or certain ganglia in the viscera are sensory in function. Those who, like myself, have implicit faith in the law and the prophets, as represented in physiological text-books, never dream of disputing physiological dogmas. But when I reached a certain stage in the study of this subject, I was led to enquire upon what this dogmatic assertion was based. I must confess I have not been able to find a single fact in support of it, apart from the fact that certain sympathetic nerves are afferent in relation to the spinal cord. Nay, further, in considering this matter I do not see how any evidence can ever be available as a result of experimental observation on animals. If a stimulus adequate to produce pain be employed and the animal shows symptoms of pain, no evidence is forthcoming to show in what region the pain is felt. Many experiments have demonstrated that the viscera in the conscious animal may be grossly injured without the animal evincing the slightest evidence of sensation. In this latter case all that has been proved has been that the stimulus has not been adequate, for we all know from personal experience that the viscera can manifest the symptom of pain.

II.—DEFINITION.

The purpose of this paper is to place before you some of the reasons that justify me in suggesting the following definition of pain :—

Pain is a disagreeable sensation due to the stimulation of some portion of the cerebro-spinal nervous system, and referred to the peripheral distribution in the external body wall of cerebro-spinal sensory nerves.

In this definition a distinction is made between the sympathetic nervous system and the cerebro-spinal. The clinical facts demonstrate that though stimulation of one system may react on the other, their functions are totally distinct, and, therefore, so far as the subject in hand is concerned, the symptom of pain is purely a cerebro-spinal function.

The above definition implies that the sensation of pain from whatever source the stimulation arises, is referred to the peripheral distribution of sensory nerves in the external body-wall, whether it arises in the brain (as in the rare cases where pain in a distant part of the body is an aura of epilepsy); in the spinal cord (as in locomotor ataxia); in the posterior root ganglia (as in herpes zoster); in the external body-wall, or in the viscera (as it will be the purpose of this paper to demonstrate).

The data on which the foregoing propositions are based are derived entirely from clinical observations. From what I have said, I consider that experimental observations on animals are of no use in deciding this question. It is only from the conscious human subject that reliable evidence can be obtained.

In studying this subject, there are two difficulties against which one has to be on guard. The first of these is the imperfect recollections of the site in which the patient has felt the pain. This can be avoided usually by getting the patient to note accurately where the pain was felt during a subsequent attack, or by watching the patient when actually suffering from pain. The second difficulty is a tendency for the observer to find only that of which he is in search, neglecting any symptom that does not accord with his preconceived ideas. I must confess I have found it necessary to put a control on my own observations by having them verified by a colleague. In making my observations I invariably had the most striking and important cases examined independently. Such phenomena as my colleagues could not verify I rejected, for if these sensory symptoms are to be of value they must be capable of being elicited by observers free from bias. Cases should not be recorded that are based upon recollections alone, for it is wonderful how far from the truth the memory may wander when there is a favourite theory to be advanced.

In bringing forward the arguments in favor of the foregoing definition I will deal with the subject partly in an autobiographical form, setting forth the reasons that gradually forced me to the evolution of the definition. I may say that it is more than fifteen years since the idea of this definition arose in my mind, as an explanation of certain observed facts. At first it was formulated with certain reservations and exceptions, but as time went on the difficulties and objections gradually disappeared as I employed more thorough and exact methods of observation. It was only within the last two years that the final objections were removed, and it is but recently that I have felt sufficient confidence in the truth of the definition as to justify me in publicly upholding it.

III.—THE PAIN OF THE DIGESTIVE TRACT.

For many years it had been my custom when writing down patients' symptoms to note the seat of pain, when it was abdominal by quickly drawing the lines which divide the abdomen into areas and marking the situation of the pain by a cross or by a wavy line. On glancing over these notes I was struck with the constancy with which pain was referred to certain areas. Thus in gastric affections the great majority referred the pain to the epigastrium. As amongst these patients there were a large number of cases of gastric ulcer, it seemed to me strange that if the pain were situated in the ulcer so many should have ulcers in the epigastric region. I also made this further observation, that in gastric ulcer when the pain was severe and limited, so that the patient would unerringly place her finger over its site, that the situation of the pain was constant when the patient took a deep breath and manifestly altered the situation of the stomach. Similarly the pain remained constant during peristalsis of the stomach and whether the stomach was full or empty. About this time I had two cases of gastric ulcer where the sites of the ulcers revealed at the *post-mortem* examination bore no relation whatever to the seat of pain during life—an observation which later experience has fully corroborated.

In continuing my observations on the digestive tract I found that the severe pains that accompany obstruction of the bowel never descended lower than the umbilical area when the obstruction was situated in the small intestine. Numerous causes have been assigned for the production of pain in obstructed bowel but there can now be no doubt, as I shall subsequently show, that it is due to the powerful peristalsis of the bowel. Peristalsis never occurs below the point of obstruction. It is my experience to meet with and to operate on a goodly number of cases of strangulated hernia. I usually make careful note of the site of pain in these cases. I have never yet found the severe colicky pains that are present descend lower than the umbilical area, when the obstruction was in some portion of the small intestine. In a few cases of obstruction of the bowel from other causes, I have been able to locate approximately its situation in the small intestine by noticing how far down in the umbilical area the pain was felt.

In a few cases of obstruction in the great bowel where the obstruction occurred at the splenic and sigmoid flexures I had noted that the pains descended lower than the umbilical area. But these cases are too few for me to dogmatise upon. We have, however, other means for testing where the pains due to peristalsis of the great intestine are felt. If a large enema be given and the individual requested to forcibly retain it, powerful peristalsis is set up in the great intestine. The pain resulting is invariably referred to a limited area immediately above the pubis, usually extending across the middle line.

As a result of these observations I have formulated the view that in pain due to the digestive tract, the pain is felt across the middle line of the abdomen, and in regularly descending areas according as the region affected passes from the stomach to the great intestine—the epigastric area being the region for stomach pains, the umbilical area being the region for pains of the small intestine, and the hypogastric area being the region for pains due to the great intestine. Many observations have justified the correctness of this view. One striking instance which is common to most people at various times is the fact that when colicky pains arise which convince the sufferer he is about to have an attack of diarrhœa, so long as the pains are felt in the neighbourhood of the umbilicus relief will not be at once forthcoming. But as time passes the pains gradually descend lower and lower and when they reach near to the pubis the call for relief becomes urgent and imperative.

IV.—The Pains due to Gastric Ulcer.

Arising out of this view, that the pain in the abdominal wall bears a relation to the portion of the bowel stimulated, my observations in regard to the site of pain in gastric ulcer are of importance. As I have said, I found the situation of the limited area of pain in gastric ulcer to be in the epigastric region, sometimes high up in this area, sometimes situated low down. I then formulated the view that probably the higher the pain the nearer would the ulcer be to the cardiac end of the stomach. This view has been verified in seven instances where I have had *post-mortem* examinations and in six cases where the site of the ulcer was discovered by operation. To illustrate, not only the justification of this view, but more important, its practical utility, I will cite three typical instances. A girl, aged 14 years, who had had pain after food for many months, referred the situation of the pain with great precision to a spot in the middle of the epigastric region. She was suddenly seized with collapse and severe pain over the upper part of the abdomen. There could be no doubt that it was a case of perforation of the stomach. Within eight hours we opened the abdomen, and as I had noted the situation of the pain previous to the rupture, I suggested that the ulcer would probably be found in the middle of the stomach. The incision was therefore made well to the left of the middle line. The perforation was readily met with in the middle of the stomach on the lesser curvature, stitched up, and the patient made an excellent rècovery.

In another case where I was called into consultation twenty hours after the perforation had taken place, the patient had suffered for many months from pain after food. She located the site of this pain with great certainty in the upper part of the epigastrium, over the xiphisternum. I reasoned from this that the perforated ulcer would be near the cardiac end of the stomach. The incision opening the abdominal cavity was, therefore, made as far to the left as possible. On opening the abdomen there was found a large quantity of fluid, and a considerable quantity of flaky lymph covered most of the exposed organs. The stomach was carefully searched, and we found it rather firmly adherent at the cardiac end to the posterior wall of the abdomen. We inspected the whole of the stomach except the adherent part, and there can be no doubt that the adhesions surrounded the ulcer. We resolved not to break down these adhesions, as it would have been impossible to drag this portion of the organ sufficiently far out to enable us to stitch it. The abdomen was very efficiently flushed, the wound stitched up, and the patient made a good recovery.

Another case had been under my care for ten years, for repeated attacks of epigastric pain. She consulted an eminent surgeon who wrote me stating that the patient had an ulcer in the middle of the stomach and on the posterior wall, and he recommended an operation for her relief. I re-examined the patient and made the following note: that, inasmuch as the pain is situated at the lowest part of the epigastric region, and as there is also here a limited area of tenderness of the skin, the ulcer should be found at the pyloric orifice. This latter view was verified at the operation subsequently performed.

V.—SUPERFICIAL AND DEEP CUTANEOUS HYPERÆSTHESIA.

Another observation I made confirmed me in the impression that the pain of visceral disease was felt in the peripheral distribution of a cerebro-spinal nerve was the detection of cutaneous hyperæsthesia in the areas where the pain was felt. This observation was made in 1891. A patient who had had an attack of gall stone colic, called on me, holding his arm stiffly away from his side. Asked why he carried himself in this manner, he replied that the friction of his clothes against his side caused him great pain. I had him stripped, and found an area of cutaneous hyperæsthesia extending irregularly over a large portion of the upper part of the abdomen and lower part of the chest, limited entirely to the right side. After this I examined systematically a large number of patients, and I found that frequently after an attack of pain, the skin remained hyperæsthetic for a varying period. When present, the hyperæsthesia invariably appeared in the region where the pain had been felt, and followed the distribution of the pain. Thus in angina pectoris I have found the hyperæsthesia limited to a small portion of the skin on the outer part of the left chest wall, exactly in the region where the pain was felt. With recurring attacks the pain became more severe, extending over the whole precordium, then into the armpit, and down the inner side of the arm. The hyperæsthesia extended in exactly the same way.

As a result of a very large number of observations, the following are the conclusions I have come to in regard to the occurrence of hyperæsthesia in visceral disease. It occurs in the peripheral distribution of those spinal nerves whose centres in the spinal cord are connected with the sympathetic nerves supplying the affected organ. It generally embraces portions of the distribution of more than one nerve. As it extends it does not affect the complete distribution of one nerve before appearing in the areas supplied by a contiguous nerve. Thus, in hyperæsthesia associated with heart affections, the hyperæsthesia may be present only in the skin covering the precordium, that is, in an area supplied by portions of the fourth and fifth dorsal nerves. As the hyperæsthesia extends it does not complete the distribution of these two nerves by extending round to the back. Rather it passes to the axilla and arm appearing in portions of the areas supplied by the third and second dorsal nerves.

The cutaneous hyperæsthesia occurs in two forms, a superficial and a deep. The former can be shown by lightly stroking the surface of the skin by a pin head. The deep form is elicited by lightly grasping the skin and gently pressing it between the finger and the thumb, or it can be shown by direct pressure. The deep kind of hyperæsthesia may be present when the superficial is absent, but is always present along with the superficial. I desire to emphasise the importance of this distinction, because, in the absence of the superficial form of hyperæsthesia, pressure over an organ may be assumed to cause pain in the organ, when as a matter of fact it is the sensitive skin that is eliciting the pain. Before I recognised this difference, I was much hindered in the study of this subject.

The borders of the hyperæsthesia are always ill-defined. The patient cannot accurately state where the skin becomes hyperæsthetic, and portions of skin evidently hyperæsthetic at one time, when tested a few minutes later are found not to be hyperæsthetic. This peculiarity also occurs in the hyperæsthesia due to herpes zoster and to organic lesions of the cord. Whether it occurs in all cases of organic lesions of the cord I cannot say, as my observations have been in only a few cases. This indefinite border is of importance, as it verifies Sherrington's observations of the over-lap in the distribution of spinal nerves.

VI.—ABSENCE OF SPINAL NERVES IN SEROUS MEMBRANES.

Although I was able to demonstrate that pain due to visceral disease was in many cases situated in the skin, yet there were a large number of cases that showed pain when pressure was applied over an abdominal organ when there was no sign of cutaneous hyperæsthesia. The recognition of the deep form of cutaneous hyperæsthesia accounted for a considerable number of such cases. But there was left a large residue, where there was tenderness on pressure and no cutaneous hyperæsthesia. It appeared to me that this might be due to a sensitiveness of the peritoneum, and the question arose in my mind: Was the peritoneum supplied by spinal nerves? I could get no help from anatomical works, and so I dissected a number of spinal nerves following them from their exit from the spinal cord to their final endings in muscle or skin. In not a single instance could I detect a twig entering either the pleura or peritoneum.

VII.—MUSCULAR HYPERÆSTHESIA.

For a long time I was puzzled to explain the apparent clinical fact that the abdominal organs were tender to pressure. But examining the cases more minutely I found out at last the true explanation. The organ that presents itself most readily for demonstration is the liver. Enlargement of this organ especially when it occurs rapidly, as in certain cases of heart failure, is very often accompanied with a good deal of pain, readily elicited by exerting pressure over the organ. In such cases if the edge of the liver be carefully marked out, and light pressure applied with the finger so as to produce pain, it will be found that the tender area extends much lower down than the liver edge. If, after ascertaining that there is present neither form of cutaneous hyperæsthesia, one deftly raises a portion of the muscle of the abdominal wall, on the right side, and lightly presses the muscle it will be found that it is the muscle itself that is exquisitely sensitive. Since making this observation I have been able to demonstrate that the pain which is caused by pressure over the abdomen in visceral disease and in peritonitis is entirely due to muscular hyperæsthesia when there is no cutaneous hyperæsthesia present. When a muscle is hyperæsthetic contraction of the muscle is often accompanied by pain, sometimes of great severity. This is best seen in the violent pain that accompanies the contraction of the hyperæsthetic intercostal muscles in pleurisy. I am convinced that the pain of pleurisy is due to this cause and not to the rubbing together of the surface of the inflamed pleura as is supposed by some people. My reasons for this assertion are, first that the pleura is an insensitive structure, as I shall show later, and, second, that exactly the same form of pain may arise when there is no pleurisy present. Thus after a severe attack of gall stone colic I have found the abdominal muscles extremely tender to pressure. But not only the abdominal muscles, but many of the thoracic muscles on the right side. If one lightly pressed the pectoralis major at the axillary fold the patient complained of the pain. In like manner pressure over the intercosal muscles elicited pain. The movements of respiration were extremely limited, the movements of inspiration being checked by violent spasms of the intercostal muscles. The picture of the patient was exactly that of one suffering from an attack of pleurisy. I need also only refer to the remarkable resemblance of the symptoms of pleurodynia to those of pleurisy.

VIII.—THE VISCERO-MUSCULAR REFLEX.

Of even greater significance than the muscular hyperæsthesia is the contraction of voluntary muscles due to visceral disease, which I have ventured to call the visceromuscular reflex. Although every clinical observer is familiar with the board-like hardness that the abdominal muscles assume in certain diseases, I doubt if in the whole field of clinical examination the value of any other symptom has been more incorrectly estimated. The muscles forming the abdominal wall have the power of contracting in limited sections and of remaining contracted for indefinite periods.

The limited hardness thus arising gives to the palpating hand the impression of a hard tumour or swelling of some abdominal organ. When this hardness of the muscle is accompanied by great tenderness, it is invariably assumed to be an evidence of peritonitis. One is struck in reading descriptions of cases by the remarkable variety of conditions for which this condition is mistaken, such as enlarged and tender ovaries, tumours, inflammatory exudations, localised and general peritonitis, contracted bowel. Surgeons have been known to express surprise at the mysterious disappearance of a tumour for the removal of which they have opened the abdomen.

The conditions giving rise to the contracted muscle are various. Peritonitis causes it, and as the muscle is also usually tender, these symptoms of hardness and tenderness of the abdominal wall have come to be looked upon as undoubted evidence of peritonitis. But these symptoms may be, and often are, present with absolutely no peritonitis. Thus I have found a tenderness with firm contraction of the lower part of the left rectus abdominis muscle in a case of stone in the bladder with no peritonitis. Hardness and tenderness of the recti over the epigastrium is common in gastric ulcer, and I have found these symptoms without any peritonitis. I have also found hardness over a limited area in the left lumbar region due to a tubercular ulcer in the posterior wall of the descending colon, and there was no peritonitis underlying the hard and tender muscle. In like manner wide-spread tenderness of the abdominal wall with hard contraction of the whole abdominal muscles may occur without any peritonitis. As illustrating the prevalent notions of the meaning of this symptom I will cite the following case. I was summoned to a neighbouring town to operate upon a fellow practitioner for obstruction of the bowels. The symptoms were, no movements of the bowel for two days, nor had any flatus been passed; some vomiting, but not fæcal; considerable abdominal distension with great hardness of the whole abdominal wall, and pain on the slightest pressure. Some difficulty was experienced in passing the finger into the bowel on account of the strong contraction of the sphincters. The patient had every few moments severe attacks of pain. The pain began in the left lumbar region passing forwards and downwards towards the pubis. The left testicle was very tender to pressure. From the situation of the pain and the tenderness of the left testicle I had no hesitation in recognising the condition as one of renal calculus. In my experience the pain in obstruction of the bowel is never so distinctly one sided. The inability to have the bowels moved was simply due to the violent contraction of the sphincters, such contraction, with the contraction of the abdominal muscles, being due to the renal calculus The diagnosis was confirmed by the passage of a calculus next day with immediate disappearance of all the symptoms This patient has had two subsequent attacks with a repetition of all the foregoing symptoms. The contraction of the muscles was undoubtedly due to a violent stimulus passing from the organ affected to the spinal cord. There the irritation spreads affecting not only the centres of the sensory nerves, but also the centres of the muscular nerves. These stimulated give rise to violent muscular contractions—the viscero-muscular reflex.

There are a few peculiarities of this muscular contraction. It is often long-continued, persisting for months, never relaxing. This one can understand; for, so long as the organ is diseased, so long may the stimulus be adequate to keep up the contraction. It also differs from the contraction of muscles due to stimulation from other causes. The contraction of a muscle in a limb due to—say a fracture of a bone or a dislocated joint—yields readily on the administration of chloroform. The muscular contraction arising from visceral stimulation does not, as a rule, yield readily to chloroform. Sometimes, indeed, the contracted recti add considerably to the difficulties of abdominal operations during the whole time the patient is under chloroform. Again, I have seen it persist for a considerable time when the patient is under chloroform and yield during an attack of chloroform sickness. I shall suggest a possible reason for this behaviour under chloroform later.

IX.—THE RESULTS OF STIMULATING EXPOSED VISCERA.

For a number of years I have seized every opportunity to test the sensibility of the viscera and their serous coverings in the conscious subject when the organs were exposed by operation. I have stimulated the pleura and pericardium, and, indirectly, the lung and the heart, through openings made by the removal of pieces of ribs for empyæma. In no instance have I been able to elicit any sensation of pain. The same result has followed the stimulation of the peritoneum and bowel in such cases as colotomies. In one case I had an unique opportunity for noting the response of some abdominal viscera to stimulation. I was called in consultation to see an elderly man who had an umbilical fistula. He had for years suffered from an umbilical hernia, and had endeavoured to keep it back by tightly bandaging a pad over it. The skin had ulcerated over a wide area in the neighbourhood, and the bowel had ulcerated through. When he took a drink of water, a few minutes later the water would be squirted with considerable force through the umbilical opening. We decided to resect the bowel. The patient objected to chloroform, and as the skin was gone from the site of the incision, and as the exposed muscle was not very tender, we resolved to proceed without an anæsthetic. After the incision into the abdominal cavity was made the rest of the operation was performed with an entire absence of pain with one exception. That is to say, we broke down old and recent peritoneal adhesions, we resected a piece of bowel and underlying mesentery, and we stitched the bowel and mesentery without the patient experiencing any sensation. I also pinched the bowel, the liver, and the peritoneum at different parts, and no sensation was elicited. But there were occasions when the patient groaned with pain. When we had prepared the upper end of the bowel, we laid it to one side on a warm aseptic cloth. At certain intervals a wave of peristalsis would pass down this portion of the bowel, and from being a wide and flaccid tube the bowel became a thick fleshy rod. Whenever this occurred the patient groaned. When asked what was the matter he said he felt severe pain. When asked where the pain was felt he passed his hand over the region of the umbilicus. Now the offending piece of bowel was lying at least 12 inches away from the area in which he felt the pain.

There are certain conclusions to be drawn from such a case as this. We know that the organs and tissues I found insensitive can give rise to the sensation of pain, for peritonitis is a painful complaint and so also are affections of the bowel and liver. All then that could be said was that my means of stimulation were not adequate to produce pain. But the stimulation applied was practically identical with that which we seek to find out the sensitiveness of an organ in clinical examination; namely, by applying pressure over an organ. If pressure applied to an exposed organ is not an adequate stimulus to produce pain it is a fair deduction that the pain which results from pressure over the organ covered by the external body wall is really felt in the external body wall.

When an adequate stimulus did occur in the above case, as when the bowel passed into peristalsis, the pain was not felt in the bowel but was referred to a situation some distance from the contracting bowel.

X.—Testicular Pain.

While I had thus gradually been getting a clearer insight into the meaning of the sensory symptoms associated with visceral disease, there was one readily demonstrated experiment which for years prevented me asserting the truth of this definition of pain. I refer to the result of applying pressure to the testicle. In ordinary cases where the cord is short the pains felt on applying pressure to the testicle are not readily discriminated. If, however, an individual with a long cord, where the testicle hangs down a long way from the groin be examined, the pains resulting from pressure on the testicle are readily differentiated. In such a case a pain is felt at once and readily localised over the point of pressure. A few seconds later another pain is felt gradually increasing in intensity, and gradually passing away and referred to the groin.

That the first of these pains was not due to the stimulation of the tissues of the scrotum, could be shown by pressing on them apart from the testicle. It was this fact that here there were two distinct pains one, the pain in the groin, referred, the other undoubtedly situated in the organ, that for years prevented me being wholly convinced of the truth of my definition. But like all the other objections it yielded in course of time, and from being a stumbling block to the acceptance of the definition, has become the strong argument in its favour. One day, while tapping a hydrocele I laid gently hold of the testicle, and touched its surface lightly with the canula. The patient at once winced with pain and placed his finger unerringly over the place I had touched. A few days later another patient consulted me. His right scrotum was distended with fluid which I took to be a hydrocele. On tapping the sac I wished to demonstrate to a colleague the sensitiveness of the testicle. I laid hold of the organ and scratched lightly over it with the canula. The patient felt no pain. I scratched again rather roughly yet no sensation was felt. After removal of the fluid the swelling had not altogether subsided, and, suspecting what was the matter, I persuaded the patient to be operated upon. On opening the sac I found that the case was not one of hydrocele, but was a case of omental hernia with the hernial sac greatly distended by peritoneal fluid. In the case of the hydrocele I had been touching the sensitive surface of the tunica vaginalis, in the other case I had been scratching the insensitive surface of the peritoneum. As the origin of the tunica vaginalis is identical with the peritoneum this difference in sensation appeared strange to me. When, however, I looked up the nerve supply of the testicle I found it stated that the genital branch of the genito-crural nerve is distributed to the tunica vaginalis. This I hold to be a very striking testimony in favour of the definition. The tunica vaginalis, I believe, is the only serous membrane that receives a cerebro-spinal nerve, and the tunica vaginalis is the only sensitive serous membrane.

In certain cases the tunica vaginalis becomes hyperæsthetic. The pain from renal calculus, as is well known, shoots into the testicle. As a matter of fact, it is in the tunica vaginalis that the pain is felt. This is readily shown, as in many cases the covering of the testicle becomes exceedingly sensitive to the lightest touch, while the tissues of the scrotum are not tender. Very frequently there is also an area of hyperæsthesia over the lower part of the abdomen, on the same side, in the field of distribution of the twelfth dorsal nerve, or upper lumbar nerves. The nerve supplying the tunica vaginalis comes from the upper lumbar nerves. The tissues of the scrotum, on the other hand, being supplied by the sacral nerves, are never hyperæsthetic in renal calculus. So distinctive is this hyperæsthesia of the tunica vaginalis that I have come to look upon it as a diagnostic symptom in doubtful cases of renal calculus.

XI.—The Mechanism by which the Sensory Symptoms in Visceral Disease Arise.

The manner in which the sensory symptoms in visceral disease arise has been described by several writers in dealing with referred pain. The stream of energy that passes to and from the viscera and spinal cord, as a rule, do not excite any consciousness in the subject. When from any cause an excessive stimulus passes from the viscera to the spinal cord, an excitation of the centres of other nerves occurs. As a consequence of this excitation, certain phenomena arise, according to the nature of the functions of the centres stimulated—it may be in the excessive action of some secretory gland; it may be in such a complicated reflex as vomiting; it may be in strong muscular contractions; it may be in such sensory symptoms as pain and hyperæsthesia. These symptoms may appear in parts remote from the organ in which the stimulus arises.

There is one other point in regard to pain and hyperæsthesia that merits some consideration. The impressions that pass from an area of hyperæsthetic skin reach the cord, while the sensory centres are in a disturbed condition. The result of the stimulus is very different from that which would have arisen under normal circumstances. What would have been recognised in health as a touch gives rise to the sensation of pain. The point I wish to emphasise is this. Stimuli arising from other organs that usually pass unnoticed may give rise to the sensation of pain when the sensory centres are thus disturbed. A patient with marked cutaneous hyperæsthesia over the upper part of the abdomen, due to gall-stone colic, felt severe pain on the ingestion of food into the stomach. The history of the patient showed there had been no actual stomach lesion. With the disappearance of the cutaneous hyperæsthesia the gastric pain disappeared. It seems that in such a case the stimuli arising from the ingestion of food, which ordinarily passes unperceived, reach the cord while the sensory centres are in an intensely excitable condition. The stimulus has, therefore, an exaggerated effect upon them, and as a result pain is manifested in the peripheral distribution of their nerves. I mention this to illustrate the fact that the functions of one organ may give rise to pain, while the actual lesion is situated in an organ more or less remote.

XII.—Some Theoretical Considerations.

If the definition I have enunciated becomes established it will necessitate the modification of some of the views held in regard to the relationship of the sympathetic and cerebro-spinal nervous systems. In Quain's Anatomy it is stated that the sympathetic nerves and ganglia are merely outgrowths of the cerebro-spinal nervous system. The following train of reasoning arising out of the facts I have detailed to-night suggests that on the contrary the sympathetic system may be the older, and that the cerebro-spinal system is built up in the first instance for the protection of the sympathetic. I think it may be taken as a fairly well-established fact, that the more recent the development of an organ the more liable it is to be affected with disease compared with older established organs. This statement has been elaborated by several competent writers in regard to disease of the nervous system, and the proneness of the cerebro-spinal system to disease has been compared to the comparative immunity of the sympathetic from gross lesions. But I should like to present a similar idea in a different form. In the administration of certain drugs, as chloroform, the manner in which they invade the system seems to be by a process of selecting the most recently-acquired functions, the one after the other. If, in the administration of chloroform, the process of abolishing all the more recent functions can be carried out until we produce a total suspension of the sensory and voluntary muscular systems, so far as they are dependent upon external stimulation, while the vital functions, as evidenced by the movements of the circulation and respiration, continue. In these functions the sympathetic system is largely employed, and it continues its work uninterruptedly while the greater part of the functions of the cerebro-spinal system is in abeyance. I have already remarked on the continuation of the muscular contraction under chloroform anæsthesia, when the stimulus producing this contraction arises from stimulation by means of a sympathetic nerve. The voluntary muscles engaged in the movements of respiration are still active so long as the stimulation reaches them from the viscera. Such a view suggests the following speculation. In the early development of animal life there is first evolved a digestive cavity, then later a rudimentary circulatory system. To these is added a rudimentary respiratory system. To co-ordinate these different systems, a nervous communication is developed which I suggest is the basis of the sympathetic system. The various organs are protected first by an insensitive, and, it may be, a somewhat unyielding outer covering. As development proceeds, this outer covering becomes modified in such a manner as to provide for both protection and movement. Then arises the sensori-muscular system. Protection is secured by rendering the outer covering sensitive, and by intimately connecting the sensory nerves with the muscles in what we call reflexes. In this manner, painful stimuli excite the muscle to contract, so that the organism is thereby removed from the offending neighbourhood. That such a view is probable, is seen in the development of the testicle. When this organ is cast forth from the protection of the abdominal wall, it is provided with an extremely sensitive covering. The tunica vaginalis like the cornea, produces with the lightest stimulation only the sensation of pain. The nerve supplying the tunica vaginalis is associated in its origin in the spinal cord with the nerves supplying the powerful psoas and iliacus muscles, so that the lightest stimulation of the tunica vaginalis provokes the immediate contraction of these muscles, and the removal of the organ from the cause of offence.

Such, in brief outline, and in a somewhat desultory fashion, is the result of my observations. I could amplify the examples indefinitely from observations drawn from other organs, but as no mere statement of mine will finally establish the truth of this definition, I refrain from elaborating the argument, leaving it to each observer to find out whether the facts are as I have stated.

Reviews.

(1) *Care and Treatment of Epileptics.* By William Pryor Letchworth, LL.D. New York, 1900.

(2) *Transactions of the National Association for the Study of Epilepsy and the Care and Treatment of Epileptics*, vol. i. Buffalo, 1901.

These two volumes are an outcome of the great and increasing interest in the welfare of epileptics which is manifesting itself in the United States of America. The work by Mr. Letchworth, who is a Past President of the New York State Board of Charities, gives a complete account of the epileptic colonies in Europe and America, and a valuable chapter upon the general principles which should guide those more immediately concerned in the development and management of such institutions. The work has required an immense amount of investigation and care in its construction. All the existing colonies on this side of the Atlantic have been visited, and important information given upon each of them. Largely as the result of the interest which many physicians in the States and others have shown in the colony treatment of epileptics, and fostered by the publication of articles in medical journals and by the direct appeals from Boards of Charities, it was decided in 1898 to form a National Association for the Study of Epilepsy and the Care and Treatment of Epileptics. This Association held its first meeting in Washington last year, and we have before us the published Transactions. The volume contains a number of interesting papers dealing largely with the colonies and special institutions existing in the United States, and two papers deal especially with the provision for the care of epileptics in the United Kingdom, and an account is given of the Chalfont colony, in Buckinghamshire, which is the property of the National Society for the Employment of Epileptics. It may be pointed out that neither of these volumes is, or contains anything in the nature of, a medical treatise upon epilepsy; but that they record observations and information respecting the history and work of existing institutions for the treatment and care of epileptics.

In connection with these two volumes, a few words may be said upon the general principles involved in the treatment of epileptics in colonies, and to consider how far they are likely to exist as independent institutions. It is, however, quite necessary at the outset to point out that the general principle involved in the foundation of colonies for epileptics should be the care, management and treatment of the sane as contrasted with the insane epileptic. But it is well known that owing to the close relationship between epilepsy, idiocy and imbecility in early life, and with dementia in the later years, it is not always possible to draw any strict line of demarcation. There are, however, numerous epileptics visiting the out-patient rooms of the general and special hospitals, and in the wards of the Poor Law infirmaries, who, if suitable opportunities were afforded them, would be capable of contributing to their maintenance. The great mistake seems to lie in depriving the epileptic child of preliminary education. In this respect the epileptic is at a disadvantage compared with the blind, deaf mutes, and feeble-minded and defective children. The epileptic is in this predicament: unless he becomes insane or is from the outset feeble-minded or becomes a pauper, neither charity nor the State makes any provision for his maintenance. It is from the consideration of such facts as these that attempts are being made by various institutions, charitable and other, both in this country, on the Continent and in America, to do something to assist the confirmed epileptic. The solution of the problem is the foundation of colonies for epileptics. Into these institutions are taken epileptic children, with the view of affording them an education in accordance with the peculiarities of their affliction, epileptic youths and adults, with the object of providing them with employment of a kind specially suitable to their disease; and epileptics convalescent either from ordinary acute illness or from the immediate effects of their peculiar malady.

As already mentioned, the epileptic has not yet earned the protection of the State, but there exist several ways by which an epileptic colony may be satisfactorily financed. The first place is given to private benevolence; secondly, as the education of epileptic children is as much a matter for the educational authorities as that of normal individuals, and as it is in the majority of cases advisable that epileptic children should be educated apart from the non-epileptic, and preferably in colonies for epileptics, School Boards may legitimately contribute; thirdly, as epileptic colonies may relieve the Poor Law authorities of able-bodied epileptics detained in workhouse infirmaries, the guardians should have the power to pay for such persons in epileptic colonies, as well as to assist relatives to maintain an epileptic member of their family in one of the colonies without at the same time pauperising such individuals; and, fourthly, by payments from the colonists. So far colonies have only been provided for the poor, or for persons of small means; but if this system comes to hold its own as the most satisfactory method of dealing with confirmed epileptics, it will be necessary to provide accommodation for those for whom high payments may be made.

It may be fairly claimed for the colony system that it provides the most satisfactory means of dealing with epileptics, both in the earlier stages of the disease and when it has become confirmed. The effect of removing the young epileptic temporarily from the ordinary occupations of life and placing him under the influence of the colony system would seem to be productive of much good towards the amelioration of his condition. The experience at the Chalfont colony in this connection has not been sufficiently extensive to permit of definite statements being made, but our observations would point to highly satisfactory results as likely to accrue from this method. The colony system is also of immense general value, for it offers the means of employment to a class of the community who have difficulty in finding work on account of their malady. It provides that kind of occupation which is most suitable for the nervous condition associated with the disease, as the work performed is scheduled and under direct supervision. The least active or alert have a fair chance of success, and perhaps of most value is the general salutary influence of the system upon the individual colonist.

From the interest which is taken in the colonies for the care and management of epileptics, full details of which will be found in the two volumes heading this review, it is the opinion of the writer that the system has "come to stay."

WILLIAM ALDREN TURNER.

Anatomie des Centres Nerveux. Par J. DEJERINE, Professeur Agrégé à la Faculté de Medecine de Paris; Médecin de la Salpêtrière; Membre des Sociétés de Biologie, de Neurologie, &c., &c., avec la collaboration de Madame Dejerine-Klumpke, Docteur en Médecine; Ancien interne des Hopitaux de Paris; Membre de la Société de Neurologie; Laureat de l'Institut et de l'Academie de Médecine. Tome ii., fascicule i. Anatomie du Cerveau (*suite*), Anatomie du Rhombencéphale. With 465 figures in the text, 180 of which are coloured. (Paris, J. Rueff, Editeur, 106, Boulevard Saint-Germain. 1901.)

THE first volume of Professor Dejerine's great work on the anatomy of the nervous centres was published in 1895. After several introductory chapters on the methods of study and development of the nervous centres, and on the general histology of the nervous system, it was occupied with the morphology of the cerebrum, with the study of microscopic sections of the cerebrum, with the structure of the cerebral cortex and its association and commissural fibres. The present volume is devoted to the consideration of (1) the projection fibres of the cerebral cortex; (2) the connections of the infra-cortical, or basal ganglia; (3) the olfactory and optic nerves; and (4) the rhombencephalon, or that part of the brain which stands in relation to the fourth ventricle. These various sections are studied on much the same plan as was adopted in the first volume.

The projection fibres of the cerebral cortex—*i.e.*, those fibres which, taking origin in the cells of the cortex, terminate at various lower levels of the central nervous axis—are considered with great fulness of detail, which is based upon the examination of no less than fifty-three cases of secondary degeneration. Three hundred pages and two hundred and forty-nine illustrations are devoted to this subject, which even yet is not fully completed. Only those fibres which terminate in ganglia situated above the pons varolii, and those paths towards lower centres which are found above that level are considered, the further continuation of these paths and their connections within the rhombencephalon and spinal cord being relegated to the volume which is to follow. In a most minute and masterly analysis these paths are traced through the centrum ovale, the internal capsule, and the cerebral peduncles. Definite portions of the optic thalamus are proved to be connected with definite areas of the cerebral cortex, and an important addition has been made to our knowledge of the connections with the corpus striatum, the geniculate and quadrigeminal bodies, and the ganglia of the subthalamic region. The pes pedunculi, similarly analysed, is shown to consist entirely of fibres derived directly from the middle sector of the cerebral cortex—that is to say, the Rolandic area and the greater part of the temporal convolutions, the bundle of Turck arising entirely from the latter. These peduncular fibres have no origin from the corpus striatum. This section is illustrated by the detailed examination of a large series of brains, some with extensive, others with limited degenerations of cortical and subcortical areas, and of other brains which have been imperfectly developed; and the section is brought to a close with a discussion of the question of cerebral localisation, and with the projection fibres of the olfactory lobe.

The connections of the corpus striatum, the optic thalamus, and the subthalamic region are considered very fully, one hundred and five pages being devoted to them. The olfactory and optic nerves are treated in a chapter by themselves, apart from the other cranial nerves, as they form definite prolongations of the cerebrum itself. One would readily have welcomed an even fuller account of the optic nerve and its connections than the author has seen his way to furnish.

The concluding chapters are devoted to the study of the topography, structure, and texture of the rhombencephalon. The topography structure of the cerebellum is treated most exhaustively, and very fully illustrated.

The volume under review, the scope of which has thus been briefly indicated, more than fulfils the anticipations founded on the study of its predecessor, and which were expressed by the present writer in BRAIN, vol. xix. It is no exaggeration to say that, alike in its fulness and masterly handling of detail, and in the number, artistic excellence, and scientific accuracy of its illustrations, it stands unrivalled among books on the subject. One who has mastered its contents, especially with the aid of sections such as these figured so largely, will have a very complete knowledge of the anatomy of the brain. Fine as were the illustrations in the first volume, they are much surpassed in technique of drawing and in the manner of reproduction by those of the present one. The majority of the drawings are original, and have been made by the aid of a camera lucida from preparations of the author's. A personal opportunity for comparing these drawings with the originals enables the present writer to speak to their marvellous accuracy. Professor Dejerine has done wisely to prefer this method of illustration to the false precision of photography.

Its author and his distinguished collaborateur, Madame Dejerine-Klumpke, are to be congratulated on the production of such an exhaustive work, which, in the writer's opinion, is destined to become the classic on the subject. It ought to form part of the equipment of every neurological and anatomical laboratory.

ALEXANDER BRUCE.

La Forme Spasmodique de la Syringomyélie, la névrite ascendante et le traumatisme dans l'etiologie de la syringomyélie. Par le DR. GEORGES GUILLAIN. (Published by G. Steinheil, 2, Rue Casimir-Delavigne, Paris, 1902.)

THE first portion of this work deals with a form of syringomyelia which the author considers has special claim to be recognised as a definite type and to which the adjective spastic has been attached. But although this spastic form of syringomyelia with its clinical features has not been described, the author fully recognises that certain spastic phenomena have not escaped the attention of neurologists.

Critzman describes this form of syringomyelia as resembling amyotrophic lateral sclerosis and other authors have described similar cases, but although the condition has been recognised pathologically, yet authors have not associated it with a definite clinical picture.

Five cases of this form are described with an autopsy and pathological investigation in two. The general attitude assumed by these patients is very characteristic: the arms hang parallel with the trunk, the fore-arm more or less flexed on the upper arm, the hand held in front of the pubis; the shoulders are raised, pushed somewhat forward; the head inclined forward. The external border of the trapezius often stands out very markedly and the supra-clavicular fossæ are deep; the whole attitude suggests one of rigidity and is similar to that seen in paralysis agitans. Special attention is directed to the position of the hand, which is said to resemble that assumed by the preacher. The hand is dorsi flexed on the fore-arm, the three last fingers flexed into the palm of the hand while the index finger is more extended.

If, in association with the position above described, there is very marked loss of power in the upper and lower limbs with exaggerated reflexes and thermo-anæsthesia, the diagnosis of the spastic form of syringomyelia is clear.

The author discusses the differential diagnosis from amyotrophic lateral sclerosis, from fracture dislocation, from caries or cancer of the vertebræ. He does not consider that a differential diagnosis can be established between a cervical pachymeningitis and the spastic form of syringomyelia, for the two conditions may be present at the same time and due to the same cause.

The diagnosis from syphilitic myelitis is fully discussed and especial emphasis is placed upon the points to which Marie has called attention. It is, however, rare to find a syphilitic meningomyelitis in the cervical region.

Chapter VI. is devoted to pathological anatomy and figures and detailed description are given of the spinal cord in two cases. The degeneration of the crossed pyramidal tracts is very marked. The affection of the cord is most marked in the cervical region and here the posterior columns are almost completely destroyed.

The author, therefore, considers that both from a clinical and pathological standpoint, a spastic form of syringomyelia may with justice be described.

The second portion of the paper deals with the part played by an ascending neuritis and traumatism in the etiology of syringomyelia—for it may be said that although the symptoms and pathological anatomy are relatively well-known, the etiology of the disease is practically unknown.

The author expresses the opinion that affection of the spinal cord may take place by way of the peripheral nerves—*i.e.*, an ascending neuritis may cause a syringomyelia, and also that traumatism plays an important part in the origin and course of certain cases of syringomyelia.

With regard to the effect of ascending neurites, the following case is recorded: A man, aged 29, previously healthy, pricked his left hand, and an abscess developed. During the following year, progressive muscular atrophy of the hand, forearm, and arm developed. When 37 years old, he was examined by Madam Dejerine-Klumpke, who at that time found muscular atrophy of the hand, forearm, arm, and shoulder, with alteration of sensibility to pain, and temperature in the hand and forearm. Twelve years later he was again examined, and at that time there was marked scoliosis, deformity of the thorax, atrophy of the hand, forearm, arm, and left shoulder, with trophic changes in the skin, and there was thermo-anæsthesia not only of both upper arms, but also of the trunk. The diagnosis of syringomyelia seemed certain, and in considering the various phases of the affection, how, little by little, the neuritis, secondary to the suppuration in the hand, ascended to the brachial plexus and to the spinal cord, it may with reason be suggested that a syringomyelia was thus developed.

There is in this case a typical example of the propagation to the cord of the inflammatory process by way of the peripheral nerves.

Numerous other cases reported by various authors are cited, proving the same point—viz., that syringomyelia may follow on peripheral injury. Some experimental evidence is then quoted, which is by no means so convincing as the clinical observations.

Siesler applied caustic to the sciatic nerve producing a complete paralysis, which terminated in the death of the animal, and at the autopsy a focus of inflammation was found at the point of emergence of the sciatic. A. Marie has shown that if a certain dose of tetanus toxine be injected into the sciatic nerve of an animal, a fatal result ensues, while, if previous to the injection of a similar dose of tetanus toxine, the nerve be divided, the fatal result does not occur.

The lymphatic circulation of the peripheral nerves is distinct from that of the surrounding tissue, and it seems to be well founded that there is a close anatomical connection between the lymphatic circulation of the nerve and that of the cord, and this explains the possibility of an infection of the cord by way of the peripheral nerves, and the author considers that he has demonstrated the possibility of a syringomyelia following on a peripheral infection.

Passing to the second etiological factor—viz., the effect of injury in the production of syringomyelia, numerous cases are quoted in which symptoms developed, as a direct effect of some traumatism.

The important work of Minor, who has shown that syringomyelia may follow on a hæmatomyelia is referred to, and also that of Van Giesson, who has given the name "hæmatomyelopore" to those cases with cavities of traumatic origin, in which the symptoms are of sudden onset, and remain stationary, whereas in syringomyelia the symptoms develop slowly and are progressive.

The author believes that traumatism is a frequent cause of syringomyelia, but all cases of hæmatomeylia do not become cases of syringomyelia.

The question whether syringomyelia may be due to some obstetrical injury is next dealt with, and evidence is brought forward showing that the condition not infrequently occurs with difficult labour; but although the seat of this lesion and syringomyelia tends to be the same—viz., the cervical region, it cannot be asserted that such birth injuries are the cause of syringomyelia in later life. The presence of blood pigment in the wall of the cavity does not necessarily prove that the cavity is of hæmorrhagic origin, for hæmorrhage may occur into a syringomyelic cavity.

The author believes that the *rôle* which traumatism plays in the production of syringomyelia in some cases is as clear as the part played by ascending neuritis in the production of syringomyelia in others; and these conclusions are not only of theoretical interest, but have a very real importance from a medico-legal point of view.

FREDERICK E. BATTEN.

A Text-book of Insanity. By CHARLES MERCIER. (London: Swan Sonnenschein, 1902. Small 8vo, 6s.)

THIS book presents the usual characteristics of Dr. Mercier's work, keenness and originality of thought, closeness of reasoning, and perfect clearness of style. The distinction which the author always shows is present here in full measure. Coming as it does immediately after his longer work, "Psychology, Normal and Morbid," we expect it to be a practical supplement to that work. In the preface we are told that this little book is intended for students whose guides in this subject have hitherto been too bulky and voluminous. "Moreover," says the author, "I was anxious to put forward the distinction that I have drawn in this book between forms of insanity and varieties of insanity, a distinction which, I think, goes far to solve the difficulties of classification."

The book is divided into three parts: The Institutes of Insanity, Forms and Varieties of Insanity, and Legal Relations of Insanity. The first part deals in four chapters with Conduct, Mind Certifiability, and Causation. The author insists upon the importance of conduct. "Special stress," he tells us in the preface, "is laid upon observation of conduct, which is, in my opinion, the key to the subject." Again in the introduction—"Conduct is the main thing that is disordered in insanity." The statement is no doubt true and it is important, chiefly because it seems to keep the observer to plain practical points; but if we give, as Dr. Mercier appears to do, the fullest extension to the term conduct and make it cover not only, like Matthew Arnold's morality, three-fourths of life, but really the whole scene of human activity, it is open to question whether the generalisation is not too large for practical use. A very able analysis of conduct begins with the statement, "Conduct is the pursuit of ends,' and goes on, "All life is teleological, and the great end to which all life is directed . . . . is the continuation of the race to which the individual belongs," the self-preservative activities coming next in importance. It would, perhaps, bring us too far afield if we were to ask whether the "end" of life, in this sense, can be its mere continuance, racially or individually, since the acceptance of this view—is it not merely to place the elephant on the tortoise once more? And, besides, in the long history of our earth innumerable races of living things have ceased to exist just as individuals cease to exist. Therefore, the "end" of life cannot be racial continuance any more than individual existence; the "end" of life, apparently, is the continuance of life—the existence of life—life, and so our teleological circle ends where it began. But it is more important to see that the keen reasoning of Dr. Mercier on these great philosophic points is, in a somewhat different sense, teleological. It is the explicatory reasoning of the philosopher who contemplates, as it were, from the outside, the trend of events. "Conduct is the pursuit of ends." If this means cosmical or even racial ends, it is no doubt in the widest sense true, but it seems to lead us, as Carlyle used to say, nowhither. Applied to the individual, on the other hand, the motive force of life is not the pursuit of ends. Will, desire, impulse, are not to be so explained, and while the philosophers tell us that happiness is our being's end and aim, or that the continuance of the race is the end of individual life, man, who in action is quite unconscious that he is the conduit-pipe for the stream of tendency, acts as he wills—"so fondly he believes."

appear to be only a question of degree. Though an excellent description is given of senile dementia under the heading "dementia," yet where it is referred to under causation, and under the heading "insanity of times of life," it is not sufficiently distinguished from other conditions of mental aberration occurring in old age. Yet it would appear to the writer of this notice, that there is no variety of insanity which is more distinct than senile dementia, distinct in symptoms, in course, and in pathological anatomy. The classification cannot be perfectly natural which associates this incurable organic disease of the brain with other conditions occurring, indeed, in old age, but often quite curable.

In a chapter of the highest excellence on the causes of insanity, Dr. Mercier discusses, among other things, the question of vulnerability, predisposition, heredity. Wisely, no doubt, he has not returned to this point with regard to classification, for the Continental authors who have endeavoured to differentiate hereditary and degenerative insanity do not seem to have fully proved their thesis.

The last part of this book, which treats of the legal relations of insanity, is probably sufficient though short, and deals with this intricate subject in a very clear and able way.

In his preface, the author has, as it were, challenged criticism on certain points on which we therefore dwell, and, as they are moot points, freely express dissent. But his claim to credit for brevity must be admitted, and no critic can but admire his terseness and vigour, and the clear emphatic style so valuable in a book for students.

Space does not allow of reference to the numerous keen and original observations scattered through the volume. Treatment is not separately dealt with, but many valuable therapeutic notes appear throughout. "Neurologists," says Dr. Mercier, "who are frequently consulted about cases of insanity, though it is a subject of which they have no special knowledge, almost invariably advise that the patient should travel. . . . Travelling is, however, almost always detrimental in the early stages of insanity." Perhaps he might have gone a little further, and referred to cases of acute melancholics who ought to be in their beds, and who are trotted round to various diversions till they are driven to suicide or worse, to incurability.

CONOLLY NORMAN.

PROCEEDINGS OF THE NEUROLOGICAL SOCIETY OF LONDON.

A paper by Dr. James Mackenzie on "Pain" was read before the Neurological Society on October 23, 1902, and appears at p. 368 of the present issue.

Writers of "Original Articles and Clinical Cases" are supplied free of charge with 50 copies reprinted in the form in which the paper stands in the pages of "Brain." If reprints are required in pamphlet form, with wrapper, title page, &c., and re-numbered pages, they must be ordered, at the expense of the writers, from Messrs. BALE, SONS & DANIELSSON, Ltd., 83-89, Great Titchfield Street, London, W.

BRAIN.

PART IV., 1902.

Original Articles and Clinical Cases.

SOME OBSERVATIONS ON PRIMARY DEGENERATION OF THE MOTOR TRACT.

BY F. W. MOTT, M.D., F.R.S.,

AND

A. F. TREDGOLD, L.R.C.P.LOND., M.R.C.S.ENG.

LATE TECHNICAL RESEARCH SCHOLAR OF THE LONDON COUNTY COUNCIL

(From the Pathological Laboratory of the London County Asylums)

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CASE NO. 1.

A case of *amyotrophic lateral sclerosis* of fifteen months' duration. General muscular wasting beginning and more pronounced in arms and hands. Exaggerated reflexes. Loss of sphincter control. Later pronounced bulbar symptoms. Extreme general wasting and great helplessness. No sensory symptoms. *Microscopically.*—Degeneration of large cells of motor cortex and of efferent tract through capsule, pons, medulla, and spinal cord, also in fibres of corpus callosum. Tangential, super- and interradial cortical fibres not affected. In the medulla atrophy of cells of ninth, tenth, eleventh, and twelfth nuclei. In the cord atrophy of anterior horn cells in lateral and postero-external groups of cervical and lumbar regions. Degeneration of fibres in anterior commissure and in antero-lateral ground bundles. No change in posterior columns. Atrophy of peripheral nerves and of muscles. Vessels in a condition of slight arterio-capillary-fibrosis.

Clinical History.[1]

E. H., female, aged 33. Admitted to Claybury Asylum for general paralysis, November 11, 1895. Unmarried; occupation, general servant. She says that up to a year ago she had been able to do her work quite well. She then noticed that her hands became weak. Although her speech is thick and indistinct, she gives perfectly rational answers to questions. Her memory, she says, is not so good as it was, and she and her friends have noticed a progressive defect in her speech. She has a small head and large projecting chin, and this, taken with her lachrymose condition, gives her an imbecile appearance, although, on conversation with her, it is apparent that she cries because of her helpless condition. The pupils are equal and react to light and to accommodation. There is a marked wasting of the muscles of the hand and forearm, with a condition of *main en griffe*, rendering her quite helpless. The thenar and hypothenar eminences are particularly wasted; also the interossei. She is unable to extend the fingers. The muscles of the body are generally wasted, but the shoulder muscles not in particular. The respiratory movements are mostly diaphragmatic, the upper part of the chest moving very little. There is a general wasting of the muscles of the leg, and a tendency to foot-drop and inversion. There is very marked foot-clonus, patellar clonus, and wrist-tap contraction obtainable. She has lost power over her sphincters, and she has some difficulty in swallowing and masticating her food. She protrudes the tongue with difficulty when asked, and she cannot protrude it far beyond the teeth; it is tremulous. There is no loss of sensibility. The muscles were tested with the faradic current, and responded; but a stronger current than usual was required. A systematic examination was impossible, owing to the patient's lamentation.

November 26.—Patient is much weaker; bulbar symptoms much more manifest, both in difficulty of speech and swallowing. She is very emotional, and continually cries out for water. She still goes about the ward wheeled in a chair. The left pupil is rather larger than the right, but they react to light and accommodation. Her craving for water is no doubt due to polyuria, for she is always wet.

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[1] Reprinted from *The Archives of Neurology*, Vol. I., p. 859.

January 29, 1896.—Patient is much feebler and more helpless, muscular wasting more marked. Knee-jerks and wrist-tap contraction very exaggerated. Can feel the lightest tactile sensation on the leg; can protrude the tongue between the teeth, but the speech is much more muttering and indistinct, although she seems to know what she wants. She is now unable to swallow even minced food. She passes a large quantity of water under her, which cannot therefore be measured. She continually asks for water. Her extremities are cold, and she is evidently sinking fast. A few days later she was affected with ulcerative colitis from which she died.—F. W. Mott.

Autopsy and Notes by Dr. Stansfield, February 13, 1896.

Muscles wasted; skull symmetrical, thick; dura mater slightly thickened; pia-arachnoid somewhat opaque and thickened; Pacchionian bodies numerous at vertex along mesial line; convolutions large, simple; sulci shallow; cortex small in amount, fair consistence, pink, striation marked; ependyma smooth. *Cord.*—Recent hæmorrhage round the dura in cervical region, the clot being dark and soft, extending from 4th cervical to 5th dorsal; cord soft, flabby, wasted in the cervical and upper dorsal portions. In the region of the lumbar enlargement it is much firmer, and there is no apparent wasting. Muscular tissue of heart very soft, brown, and small in amount; weight, 5 oz. *Liver.*—39 oz.; slightly fatty. *Spleen.*—4 oz.; firm. *Kidneys.*—9½ oz.; capsule slightly adherent. Large intestine congested throughout its entire length. Two ulcers in the first part of rectum, one large, about ¾ in. in diameter, with thick, overhanging margins.

Cause of Death.—Ulcerative colitis and dementia of general paralysis. (Microscopic examination and the smooth ependyma of the ventricles showed that this was not a case of general paralysis.—F. W. Mott.)

Microscopical Examination.

Brain.—The large pyramidal cells of the third layer are diminished in number, and many of those which are present show important pathological changes. Many of them have quite lost their normal shape, and are swollen and globular looking; others are shrunken and atrophied. In many instances the nucleus and cell processes are very indistinct; most of the cells also contain a large amount of yellow granular pigment. These degenerative changes are confined to the large cells, the small and medium-sized pyramids being quite healthy. Throughout all the cortical layers small round cells and Deiters' cells are present in large numbers, but especially so in the deepest polymorphic and granule layers. An examination of Marchi-stained sections shows that there are large numbers of degenerated fibres throughout the white substance, and also in the corpus callosum, most of such fibres being of large size.

The tangential, super- and interradial systems of fibres are well seen, and show no change; indeed, a particularly abundant layer of tangential fibres is present.

The pia-arachnoid is thickened in places, and its vessels are distended. Fatty changes are also present in many of the capillaries of the brain, but such do not bear any relation to the areas of cellular degeneration.

Internal capsule.—There are many fibres undergoing recent degeneration, but carmine and Weigert preparations do not reveal any definite area of sclerosis.

Crura.—Many fibres undergoing degeneration occur in all parts of the pes, and at this level definite interstitial sclerosis can for the first time be made out, especially in the mesial portion.

Pons and Medulla.—Recent degeneration, with slight interstitial overgrowth, occurs throughout the efferent tract. There are also well-marked degenerative changes in the cells of the ninth, tenth, eleventh and twelfth cranial nerve nuclei.

Spinal cord.—Cervical enlargement (C. 2, 3, 4, 5, 6, 7, and 8, D. 1 and 2). At all these levels there is recent (Marchi) degeneration with interstitial sclerosis in the crossed pyramidal tracts. Some slight sclerosis exists in the direct tract, which, however, cannot be traced lower than the second dorsal segment. There is also a little degeneration in the lateral ground bundles, which is probably due to the involvement of commissural fibres; also a few degenerated fibres in the anterior commissure. No other portions of the white matter are affected.

The anterior horn cells are much diminished in number, and most of those which remain are undergoing degeneration. These changes do not affect all the cell groups however; the mesial-anterior group is practically normal, and the change is most marked in the lateral and postero-external groups; within these groups there are scarcely any large ganglion cells having a healthy appearance. The condition appears to be one of chronic atrophy, there being no evidence of acute change. The cell gradually becomes smaller and withered-looking; it loses its characteristic multipolar shape, and is fusiform or crescent-shaped. The chromatic substance loses that regular arrangement which is such a pronounced feature of a healthy anterior horn cell; occasionally it has completely disappeared, its place being taken by a mass of yellow pigment, which stains black with Marchi fluid. The nucleus is frequently eccentric, the nuclear membrane very ill-defined. The cell processes are fewer in number, and often broken off short, and the anterior roots are atrophied. The posterior roots show no change.

In addition to these alterations in the cells there is a very great decrease in the number of fibres composing the network of the anterior horns; such diminution is especially marked in the more central parts of the horn.

Dorsal region (D. 3, 5, and 8).—There is well-marked interstitial sclerosis in the crossed pyramidal tracts in all these segments, but the amount of recent (Marchi) degeneration is very much less than in the cervical region. Recent degeneration and sclerosis also exist in the anterior commissure to a slight extent.

The anterior horns are practically normal, it being impossible to make out any diminution in the number of cells or fibres composing them, neither can any degenerative changes be seen. The cells of Clarke's column are likewise healthy, and not decreased in number.

Lumbar region (L. 3 and 5).—The crossed pyramidal tracts show precisely similar changes to those in the higher parts of the cord, except that there is more interstitial sclerosis and less recent degeneration. There is, however, plenty of recent change in the antero-lateral columns, and also in the anterior commissure.

Alteration in the structure and decrease in the number of the anterior horn cells exist as in the cervical region, but to a far smaller extent; such changes being also most pronounced in the lateral and postero-external cell groups.

Membranes.—There is a slight thickening of the pia-arachnoid all round the cord, which is greatest on the anterior surface. The walls of many of the small and medium-sized *vessels* are slightly thickened and fibrous; the *central canal* is normal throughout.

Ulnar nerves.—Transverse sections of hæmatoxylin preparations show that in each bundle there are many fibres which remain unstained. There is also a slight increase of fibrous tissue, but Marchi sections show comparatively little recent degeneration.

Thumb muscles.—Many of the fibres have completely lost their striation, some being clear and homogeneous looking, others finely granular, and others in a condition of actual disintegration. Marchi-stained sections show that throughout the entire muscle there are many fibres in a state of fatty degeneration; in between those undergoing the above changes, however, fibres occur which appear to be perfectly healthy.

CASE NO. 2.

A case of *amyotrophic lateral sclerosis* of eleven months' duration, beginning with painful cramps, followed by loss of power in right leg. Left leg, right arm, and left arm shortly afterwards affected. General muscular wasting, most pronounced in small muscles of hands. Exaggerated reflexes. Later, loss of control over sphincters. Delirium, extreme helplessness. No impairment of sensation. Pronounced bulbar symptoms shortly before death. *Microscopically.*—Recent degeneration of projection fibres in motor area of brain, also in corpus callosum, but no alteration in cells. At level of pons sclerosis begins in pyramidal tracts and continues to the furthest extent of the cord. Cells of anterior horns atrophied in C. and L. regions, also decrease in network of anterior horns. Glossopharyngeal and hypoglossal nuclei affected. Clarke's column normal. Sclerosis in Goll's and antero-lateral columns. Universal arterio-capillary-fibrosis. Atrophy of fibres of peripheral nerves.

Clinical History.

J. G., male, aged 67; occupation, labourer; was admitted into Charing Cross Hospital under Dr. Mott, on January 3, 1898, for muscular weakness. There is nothing in the family history bearing upon the case. The patient has been a soldier, and served through the Crimean War and the Mutiny. Whilst in India he had dysentery, and also a chancre and bubo. His present illness began four and a half months before admission; he had previously been working in a white lead factory for three weeks. He first noticed a painful cramp in the right knee, which persisted and became so bad that in a month's time he was unable to walk. He then began to lose the power of movement in his right leg, and had periodic attacks of twitching and cramp in this limb; according to the patient such attacks lasted from ten to thirty minutes; he described the limb as being "all of a shake," and states that if he were standing when such an attack came on he would fall down. The left leg then became similarly affected to the right, but there was less pain; finally he lost all power of standing. Shortly after this he noticed loss of power in the right arm, and a little later the same in the left. He has suffered with constipation since the illness commenced.

On admission.—Patient is fairly well nourished, he sits propped up in bed in great distress during the periodic attacks of pain; he sweats profusely at times; complains of a disagreeable smell in the nostrils. He answers questions rationally, but is very emotional, bursting into tears when narrating his illness. He passes a normal quantity of water with a trace of albumen. His appetite is good; he complains of thirst. *Heart.*—Sounds muffled, but no murmur. *Lungs.*—Emphysematous. *Abdominal viscera.*—Nothing abnormal detected. *Nervous system.*—The patient has not sufficient power to raise or lower himself in bed, and is quite unable to stand alone. The muscles of the arms and legs generally are much wasted, but particularly the interossei and those of the thenar and hypothenar eminences of the right hand. He has great difficulty in flexing the knee joints, but can flex and extend his toes and also perform external and internal rotation of his feet. Fibrillary twitchings can be seen in the muscles of both legs and of the right arm. The deep reflexes are markedly exaggerated, knee-jerks being excessive, ankle clonus present, and wrist-tap contractions readily obtained. There is no loss or impairment of sensation to touch, heat and cold, or pain. Sense of position is likewise unimpaired. Smell, sight, hearing, and taste good and no difficulty in swallowing or talking.

January 17.—The patient now suffers considerably less pain; when present it begins at the ankle and stops at the knee, seldom reaching as high as the groin. His arms seem weaker, and he complains of being very thirsty.

February 3.—Still pains of a shooting character in the legs, right more than left. He also has pain in the right wrist and metacarpo-phalangeal joints, and the hand is slightly œdematous.

Electrical examination.—Right arm. With the faradic current, the deltoid does not respond, the interossei and the extensors of the fingers respond only sluggishly to a fairly strong current. With the galvanic current, the deltoid and extensors react normally, but require a moderately strong current; the interossei react to K.C.C., but a stronger current than normal is required. There is no reaction of degeneration.

Left arm.—With the faradic current, the interossei respond if a strong current is used; all the other muscles of the arm and forearm respond to a slightly increased current. With the galvanic current all the muscles react normally.

Legs.—With the faradic current, none of the muscles of either leg react. With the galvanic current, there is a sluggish response in all the groups, if a strong K.C.C. is used.

March 5.—Patient began to lose control over his sphincters.

March 4.—Delirious in the night.

March 14.—Complained of severe pains in the lower part of spine, for which morphia had to be given hypodermically; this pain persisted, and was so severe that the injections had to be continued constantly.

He remained in this condition for some months, then his articulation became so affected that it was impossible to understand him. A few days after the onset of this symptom he began to have difficulty in swallowing; even fluids at times caused him to choke, but they did not return through the nose. He was very emotional. Shortly afterwards, a pressure sore appeared on the inner side of each knee. He was always very thirsty, and gradually became weaker till his death on July 15, 1898, about seven months after admission.

The affection of the muscles was such that for some months before he died he was quite unable to move his arms to feed himself; their position was adduction at shoulder, flexion at elbow, and flexion of the thumbs and fingers; this position persisted until death. Six weeks before he died, right foot-drop was very marked, and both feet were œdematous, and the ankles very painful. Latterly he knew when he passed his water, but it was all passed under him. He never had any squint or affection of sight. He always complained of thirst. The temperature was normal throughout his illness, till three or four days before death.

Post-mortem Notes.

Body wasted. P.M. staining slight, and at most dependent parts only; rigidity passing off; no bed-sores.

Thorax.—Rib cartilages ossified; both lungs œdematus and deeply pigmented; emphysema along borders. Pericardium contains half an ounce of clear fluid; the membrane has several opaque patches. The heart weighs 9 oz.; muscle is normal, and the valves competent. There is extensive atheroma of the first part of the aortic arch.

Abdomen.—Mucous membrane of the stomach is atrophied. The liver is fatty and congested, and weighs 2lbs. 5oz. Gall bladder and its ducts are normal. The spleen is adherent and friable. Kidneys.—Left weighs 7½ oz., capsule is adherent, and the whole organ congested; right weighs 3 oz., and contains numerous cysts, which are filled with fragments of calcareous matter; the pyramids are wasted, and the pelvis inflamed. Bladder is small, and its mucous membrane in a condition of chronic inflammation. Pancreas is normal.

Brain.—The dura is normal; and the Pacchionian bodies are large and prominent. The sulci in the central regions are filled with opaque lymph, and the pia-arachnoid is opaque and somewhat thickened.

Microscopical Examination.

Brain.—Sections of the motor region stained by Marchi's method reveal the presence of many degenerated fibres of the projection system, many such are also found in the corpus callosum. Unfortunately the method by which the brain had been hardened made it impossible to use Nissl's stain, but in sections stained by the carmine and Weigert-iron methods there does not appear to be any alteration in the cells. The tangential and supraradial fibres are likewise normal. The pia-arachnoid is considerably thickened in places, and there is also fibrosis of the middle and outer coats of many of the small and medium-sized arteries; in many of the vessels this thickening is of a hyaline nature, but there is no endarteritis.

In the *crura* and upper part of the *pons* there is abundant recent degeneration without sclerosis of the fibres of the efferent tract; in the lower part of the pons the presence of an interstitial sclerosis becomes evident, and from thence continues downwards as far as the sacral region of the cord.

In the *medulla* there is very marked diminution in the number of cells lying around the floor of the fourth ventricle. The nuclei of the ninth and tenth cranial nerves are particularly affected; not only are there very few cells, but nearly all those which are present are in a condition of advanced degeneration, almost exactly the same as the anterior horn cells presently to be described. The nucleus of the twelfth nerve is also affected, but to a somewhat less extent.

Spinal cord.—Cervical enlargement (segments C. 2, 3, 4, 5, 6, 7, 8; D. 1 and 2). In all these sections there is very considerable recent degeneration with interstitial sclerosis in both crossed and direct pyramidal tracts; one of the latter is more affected than the other, which is evidently due to the direct tracts being unequal on the two sides, as not uncommonly happens. Within the affected areas there is a great diminution in the number of fibres, and the majority of those which remain are of small calibre, which apparently shows that the large fibres are those chiefly affected. In the lateral columns the degenerated area exactly corresponds with that of the crossed pyramidal tract, and the zone of white matter intervening between the inner border of this and the gray matter of the horn (lateral limiting layer) is perfectly healthy. There is also a similar degeneration and sclerosis in the antero-lateral columns in the form of a narrow band extending from nearly as far forwards as the direct tract to nearly as far backwards as the crossed, and lying midway between the gray matter and the periphery of the cord (fig. 2, Plate I.). This is probably partly due to degeneration of commisural fibres connecting the upper and lower limbs, as it can be traced as far down the cord as the lumbar enlargement; possibly in the cervical region it is also partly due to the atrophy of outgoing fibres from the anterior horns, as the anterior roots are noticeably affected. Recent degeneration and slight sclerosis are also present in the posterior columns, corresponding to an early tabetic lesion affecting the root zone in the lumbar region and Goll's column above.

In addition to these changes in the white matter there is a very marked diminution in the number of the anterior horn cells. This change is practically confined to the lateral and postero-external cell groups, the mesial-anterior group showing scarcely any change. Within the affected groups nearly all the cells which remain are in a condition of chronic degeneration, and of many of them all that remains is a small collection of granular pigment. The network of fibres in the middle portion of the horn as well as in the posterior commissure is also exceedingly scanty, owing to the atrophy and disappearance of a large number. Carmine-stained sections show the presence of numerous Deiters' cells and sclerotic tissue in these regions. These changes in the anterior horn cells are much more marked in the lower cervical and first two dorsal segments than they are in the higher part of the cord, that is, in that portion of the cord from whence arise the nerves supplying the arm and hand. In this region the atrophy of the anterior horns is so pronounced that it is quite evident to the naked eye.

The anterior roots are small and contain many atrophied fibres, but show very little recent degeneration.

Dorsal region (Segments 5, 6, 8, 10, and 12).—The change in the direct tract becomes much less marked at the level of the eighth segment, otherwise the recent degeneration and sclerosis in the efferent tracts is similar to that in the cervical region; the lateral limiting layer being also quite unaffected. The change in the antero-lateral columns is likewise similar in nature and situation, but in the posterior columns at the level of the tenth and twelfth segments, although the sclerosis is best marked in the inner portion of Goll's column, there is a slight interstitial increase throughout both postero-internal and external tracts.

It is quite different, however, with the anterior horns. Throughout the whole of the dorsal region these cells appear quite healthy, and are not noticeably diminished in number, neither is there any decrease in the meshwork of fibres. There is no change in the cells of Clarke's column.

Lumbar enlargement.—In these segments sclerosis is still present in the lateral columns as a very well-defined triangular area. There is also slight sclerosis in the antero-lateral columns, and a diffuse sclerosis with diminution in the number of fibres throughout the posterior columns; in the latter region it is most pronounced in Charcot's root zone and the immediate neighbourhood of the posterior longitudinal fissure, except the small oval area of Flechsig.

The anterior horn cells are affected to an even greater degree than in the cervical enlargement, and all the cell groups to an equal extent. Not only are there comparatively few cells present, but those which remain are so profoundly altered that it is with great difficulty one can find any normal cells. Of those present many are little more than globular masses of yellow granular pigment, surrounded by a clear space, and apparently quite destitute of nucleus or processes. In others the change is not quite so advanced, and although the cell is very much shrunken and its outline altered, an indistinct nucleus and short, broken-off processes can still be recognised. In the anterior horn cells throughout the cord there is a very considerable deposit of granules of yellow pigment. In no instance could we discover any indication of acute changes in the cells.

Unfortunately the spinal ganglia were not preserved, but *no change* could be seen in the posterior roots.

Vessels.—Practically all the vessels of the spinal cord and also many of the smaller ones in the membranes are much thickened; this thickening involves the middle and outer coats; in some vessels it is fibrous and in others hyaline in nature. To many of the vessels there are well-marked processes of fibrous tissue radiating outwards from the adventitia, and insinuating themselves between the nerve-fibres. The intima appears perfectly normal, and we could find no trace of hæmorrhage, embolus, or thrombus. This condition of arterio-sclerosis is similar to that described by Gull and Sutton; its presence was also noted in the brain, indeed, it is universal throughout the nervous system, although most marked in the cord.

Membranes.—In the brain there is very marked thickening of the pia-arachnoid over the motor convolutions. In the cord this membrane is also greatly thickened, but only on the anterior and lateral surfaces, no change being evident in the membrane over the posterior columns. The septa passing into the cord from the periphery are also very much thickened.

Ulnar nerves.—There is a very marked diminution in the number of nerve-fibres in all the fasciculi, their place being taken by an increase of fibrous tissue. This condition is seen in transverse and longitudinal sections. Marchi-stained sections do not show any recent degeneration.

CASE NO. 3.

A case of *progressive muscular atrophy* of over four years' duration; beginning with weakness in right arm, and a few months afterwards in left arm. Weakness and wasting of various muscles of arms and shoulders, with absent reflexes. Knee-jerks exaggerated. Speech and swallowing not affected. Admitted into hospital for severe cystitis, of which he died within ten days. *Post mortem.*—Chronic cystitis with early suppurative nephritis. Extreme degeneration of anterior horn cells in cervical enlargement, antero-internal group least affected, atrophy of anterior roots. No change in anterior horns in D. and L. regions. Slight sclerosis in posterior columns; slight sclerosis in crossed pyramidal tracts in lumbo-sacral region, no change in pyramidal tract above. Universal arterio-capillary-fibrosis.

Clinical History.

E. S., male, aged 57; cabman; was admitted into Charing Cross Hospital, under Dr. Mott, on July 14, 1896, suffering from retention of urine.

There was nothing in the family history bearing upon the case.

The present illness began a little over four years ago with weakness and wasting in the right hand. Later, in March, 1892, he was lifting a box on to his cab when he fell backwards, and the box fell on him. He was unconscious for a few minutes, but soon recovered, and then drove his cab to the station. The same day the weakness in the right arm became worse, and about three months afterwards he began to experience loss of power in the left arm. Since June, 1892, the patient has been unable to use his right arm for driving, and since October, 1892, the left arm has been useless for the same purpose.

This helpless condition of the patient led to him going the whole day without passing water, as he found difficulty in using either hand. For the last seven or eight months, however, his urine has constantly dribbled away, which he thought was due to weakness. This condition not getting better, the patient came to the hospital; it was then found that he had retention with overflow.

On making an examination of the patient, he was found to have marked progressive muscular atrophy, although he probably would not have presented himself for treatment had it not been for the bladder trouble.

At first sight it might appear that the onset of the muscular atrophy was due to the accident in March, 1892, but the patient is quite definite that he had noticed some weakness and wasting in the right hand for a short time before this. This being so, the accident was probably the effect and not the cause of the disease; further, the subsequent *gradual* progress of the wasting, and the fact that it was three months before the left hand became affected, is against the view that the disease was the result of hæmorrhage into the gray matter of the cord.

On admission.—Power of movement. In the right arm slight flexion and extension of the fingers can be performed, but not of the thumb. Extension of the wrist is entirely absent, but some power of flexion remains. Pronation and supination are absent. There is no power of flexion at the elbow, but some power of extension. At the shoulder joint abduction and adduction are wanting; slight rotation is possible; elevation is practically normal. Left arm.—Movements of the fingers and wrist are the same as in the right arm, but slightly stronger. Pronation and supination are absent. Flexion and extension of the elbow joint can be performed fairly well, and the hand can be brought nearly up to the mouth. Abduction of the arm at the shoulder can be performed; there is fair antero-posterior movement, and some rotation. In the lower limbs movements at all the joints appear normal.

Nutrition.—The interossei and the thenar muscles of both hands are much wasted, as are also the muscles of both forearms. On the left the supinator longus is well preserved. The biceps is practically gone on the right, and much wasted on the left. The triceps are still fairly preserved on both sides. Both deltoids are atrophied; the pectorals, trapezei and the serrati magni are fairly strong. There is some wasting of the muscles of the neck. The skin over the fingers of both hands is red and sticky. The right wrist joint is very lax, and allows of extension and passive movement; there is fulness over the synovial sheaths of the flexor tendons. There is some grating in the right shoulder joint on passive movement. Fibrillary twitching is observable in the muscles of the right forearm. The muscles of the legs generally are slightly wasted, but no group is especially affected.

Sensation.—Tactile sensation is slightly impaired in both legs, and in the right hand, especially over the ring finger.

Reflexes.—These cannot be obtained in either arm; in the legs the knee-jerks are very brisk, but there is no clonus.

Electrical reactions.—The reactions of the muscles of both upper extremities are diminished quantitatively. In the muscles of the thenar eminence of the right hand all reactions seem to have disappeared. All the muscles show polar changes, A.C.C. being distinctly greater than K.C.C. The contractions, however, are not sluggish. Stimulation of the muscles through the nerve trunks by galvanism or faradism produces contractions. To the faradic current the reactions of the muscles are normal, prompt contractions being produced by a moderate strength of current. Sensibility to both currents seems about normal.

Speech is unimpaired. *Deglutition* is normal.

Urine is very pale and opalescent; sp. gr. 10·10; alkaline in reaction; contains pus and albumen in considerable quantity.

July 22.—There is no change in the nervous or muscular symptoms, but patient says that he feels very weak, and he is evidently very ill. His pulse is 120; he has had persistent hiccough for the last two days; complains a good deal of pain in the umbilical region, and, in spite of energetic treatment, the cystitis still persists.

July 24.—Patient is so ill and exhausted that he speaks with difficulty. Pulse 66, very irregular and collapsing. Early this morning he had an attack of syncope, but came round on the administration of strychnine and ether. Pupils are rather irregular, the left being more contracted than the right.

He gradually sank and died the same evening, there being no alteration in his nervous symptoms.

Post-mortem Notes.

All the organs were found to be healthy, with the exception of the genito-urinary apparatus. There was well-marked chronic cystitis, the mucous membrane of the bladder being much thickened, and covered with phosphatic deposit; here and there were areas of acute inflammation; there was commencing suppurative nephritis.

Brain.—The pia-arachnoid was slightly opaque and thickened over the central convolutions. Here and there were a few small cysts, varying in size from that of a hemp to a millet seed. These might probably be due to early decomposition, or be small softenings resulting from vascular change. The ventricles were not granular, and the membranes were not adherent.

Spinal cord.—The dura mater showed no naked-eye change. The whole of the lower cervical and upper dorsal regions of the cord were remarkably flattened, and on section there was obvious atrophy of the anterior horns. The lower dorsal and lumbo-sacral portions of the cord seemed perfectly normal.

Microscopical Examination.

Unfortunately the ganglion cells of the motor cortex could not be examined by Nissl's method, but in sections of the crura, pons, and various levels of the medulla the efferent tracts are perfectly normal; indeed, the sections of the central nervous system above the level of the cord show no pathological change, with the exception of some thickening of the middle and outer coats of the smaller vessels.

Spinal Cord. Cervical Enlargement.—(C. 4, 5, 6, 7, and 8). In all these sections the cord is flattened and wasted, and the anterior horns are obviously abnormal in shape and much atrophied. Throughout the whole of the enlargement there is pronounced diminution in the number of the anterior horn cells, and those which are present are in an advanced condition of degeneration, it being almost impossible to find a healthy cell in this region. The change undergone by these cells is a chronic one, associated with the deposition of much granular pigment, precisely the same as that described in the other cases; the mesial-anterior group of cells in this case also being less affected than the other cell nests.

There is also a very noticeable decrease in the network of fibres of the central portion of the horns, the fibres lying towards the periphery not being nearly so much affected; in the middle of the horns considerable numbers of Deiters' cells are also present.

At the level of the sixth segment in one of the horns there is a small focus of softening containing altered blood corpuscles and granular masses of pigment.

The anterior roots arising from this region are small, and many of the fibres are seen to be atrophied.

There is definite interstitial sclerosis at the periphery of the cord in the antero-lateral columns, with some thickening of the adjacent pia-arachnoid membrane. Probably this peripheral sclerosis is due to the atrophy of outgoing motor fibres, rather than to the involvement of one of the tracts of the cord. The change ceases above the fourth cervical, and below the second dorsal segments; its situation also exactly coincides with the area of emergence of the anterior roots. The thickening of the investing membrane and of the septa in this region is probably also the result of irritation by products of degeneration carried outwards along the nerve roots. Slight interstitial sclerosis is also present in the intermediate portion of the antero-lateral columns; this is no doubt due to atrophy of association fibres.

Dorsal Region. (D. 3, 6, and 8.)—In these sections the anterior horns are perfectly normal, both with regard to cells and fibres. The anterior roots are also healthy. The cells and the reticulum of Clarke's column are abundant, and show no change.

Lumbar Enlargement. (L. 4 and 5; Sa. 1.)—In none of these sections is there any change whatever in the cells or fibres of the anterior horns. Marchi sections show a few black dots amongst the fibres of the anterior commissure and in the posterior columns there is slight interstitial sclerosis, indeed, both postero-external columns in all regions of the spinal cord contain many fibres undergoing degeneration,, with some interstitial sclerosis, as shown in fig. 3, Plate II. Many of these from their situation are undoubtedly endogenous association fibres, and due to destruction or degeneration of cordonal cells at the base of the posterior horn in the atrophied portion of the cord.

In all these sections through the lumbar region there is definite interstitial sclerosis with atrophy of nerve-fibres in the crossed pyramidal tracts of both sides; it is most marked in the fibres lying nearest the surface of the cord, which are probably the longest fibres in the upper efferent tract. This is of interest as showing the primary degeneration of the terminal branches of the cortical pyramidal neurones with the longest axons, and accords with the brisk knee-jerks.

Vessels.—Most of the vessels throughout the cord are in a condition similar to that described by Gull and Sutton (arterio-capillary-fibrosis), the media and adventitia being much thickened, at times fibrous, at others hyaline in appearance. Surrounding many of the vessels there is quite a thick overgrowth of fibrous tissue which extends in a stellate manner into the adjoining nervous tissue.

A medium-sized vessel on the anterior surface of the cord in the lumbar region shows pronounced thickening of the intima (*endarteritis obliterans*), but this is the only vessel showing such change which was discoverable amongst all the sections examined.

Membranes.—The pia-arachnoid is slightly thickened throughout the whole extent of the cord, but most on the anterior and lateral aspects. In the cervical region products of degeneration (myelin and fat-globules of varying sizes, and fat-carrying leucocytes) occur in considerable quantity between the membranes and the external surface of the cord.

Posterior Roots.—Many of the incoming fibres of the posterior roots in all the regions examined are degenerated; unfortunately the ganglia were not removed, so that it is impossible to say what was the condition of these.

CASE No. 4.

A case of *chronic rheumatoid arthritis with muscular atrophy* of several years' duration, beginning with pains in feet and afterwards in hands, followed by contractures. Pronounced deformities of all limb joints, especially the smaller ones, with osteophytic outgrowths and considerable muscular wasting. Sensation, speech, and swallowing normal. Death from broncho-pneumonia. *Microscopical examination.* —No change in either white or gray matter of brain, pons, or medulla. In the spinal cord chronic atrophy with excessive pigmentation of anterior horn cells in cervical and lumbar enlargements, all groups affected (especially the mesial-anterior). Decrease in fibrillary network. General slight interstitial overgrowth throughout the cord with arterio-capillary-fibrosis, but no tract degeneration; slight chronic changes in cells of posterior ganglia, atrophy of peripheral nerve-fibres, atrophy and fatty degeneration of muscles.

Clinical History.

J. D., aged 53, widow; charwoman; was admitted into Colney Hatch, February 15, 1896. Medical certificate on admission:—She is dull and depressed, she talks incoherently, and declares that other patients are spreading a number of bad reports about her, and that she can hear voices outside the ward and up in the ceiling. She thinks she is to marry the doctor, and that several children are in the ward.

She gives the following *history* of herself:—Four years ago she had pains in the feet, and then in the knees, which subsequently became contracted, preventing her walking. Two and a half years ago the hands also became affected with pains, afterwards followed by considerable rigidity of the elbow and hand.

Her *present condition* is as follows:—She lies in bed on her right side, with her chin resting on the sternum, the movement of the head being very limited.

Lower limbs.—The hips are flexed on the body, the knees are flexed, and the ankles extended. The end of the femur can be seen projecting in front of the head of the tibia, the internal condyle is prominent, the patella is thrown outwards, resting on the outer condyle; the head of the fibula projects externally; there are considerable numbers of osteophytes developed; the knee-joints are apparently ankylosed; the internal and external malleoli are prominent, and the ankle-joint is fixed; the big toe is turned outwards, but does not cover the digits. The four digits are over-extended at the metatarso-phalangeal joints, and fixed at the first interphalangeal joint, where there is considerable thickening. There is pronounced muscular wasting of the limbs.

Upper limbs.—Here the most marked deformities are in the hands. There is flexion of the ungual phalanx on the second to an obtuse angle, extension of the second phalanx on the first, and flexion of the first phalanx on the metacarpal bone; flexion to a less obtuse angle of the metacarpus and carpus on the bones of the forearm. There is ulnar deviation of the hand, and a prominence of the first metacarpo-phalangeal joint. The forearm is pronated, and the elbow flexed. The shoulder joint is rigid, and the upper limb is fixed to the chest in a position of adduction. The finger-nails are small and atrophied.

There is great nodular deformity about the metacarpo-phalangeal joints and the wrist, and all the muscles are much wasted. The skin of the hands is smooth, red, and cold, and has lost its wrinkles, but there is no loss of sensation.

The muscles most wasted are the small muscles of the hand, forearm, arm, foot, leg and thigh, in the order mentioned. All these respond readily to faradism. K.C.C. is less than A.C.C. There is no fibrillary twitching.

There is no loss of sensation, and no loss of control over the sphincters. The diaphragm during respiration contracts rather more forcibly than is usual in a woman. There is no affection of speech or of swallowing. (F. W. M.)

No change occurred in her mental and physical condition, and three months later she died of broncho-pneumonia.

Post-mortem Examination.

It was found to be quite impossible to move the joints out of the abnormal positions which have been described. There were no bedsores.

The brain appeared fairly normal, and sections showed no naked-eye change; several portions were preserved for microscopical examination. The membranes were not thickened, nor were they adherent.

The spinal cord showed no naked-eye change; it was preserved with several of the spinal ganglia for further examination.

Heart.—Small, weighing only 6 oz. No valvular lesion, muscle substance of a dark reddish colour, contrasting in this respect with the atrophied skeletal muscles.

Lungs.—Pneumonia and recent pleurisy of the right upper lobe. *Liver.*—Very large, 64 oz., nutmeg appearance on section, did not give the iron reaction. *Kidneys.*—6½ oz. the pair, very pale and obviously fatty, especially the cortex. *Spleen.*—4 oz., pale and somewhat diffluent.

The atrophied limb-muscles were very pale, and appeared to be infiltrated with fat.

Microscopical Examination.

Brain.—Motor cortex. Sections stained by Nissl's method show no pathological change whatever in the cortical cells. The vessels are healthy, and there is no thickening of the membranes.

The *internal capsule, crura, pons, and medulla* likewise appear perfectly normal.

Spinal cord.—Sections were examined at the level of the sixth, seventh, and eighth cervical; first, tenth, twelfth dorsal; second and fifth lumbar, and first sacral segments.

Gray matter.—In the cervical enlargement there are very important alterations in the large cells of the anterior horns. There are fewer such cells present than in the normal cord in this region, and a large number of them are seen to be undergoing a chronic degenerative change, with the deposition of a large amount of pigment, just like the change occurring in Cases No. 1, 2, and 3. In the present case, however, it does not appear to be quite so extensive, and there are some fairly healthy cells scattered amongst the atrophied ones; the process also does not pick out any special group of cells as in the other cases, but affects apparently to an equal extent all the different groups.

In the dorsal segments examined there is not anything like the same amount of change in the anterior horn cells; here and there degenerated cells occur, but they are comparatively rare, whereas in the cervical and lumbar parts of the cord the reverse is the case, and healthy cells are in a decided minority.

In the lumbo-sacral portion of the cord exactly similar changes occur as in the cervical enlargement, that is, many cells in various stages of degeneration are scattered throughout all the cell nests.

The mesial-anterior group certainly appears to be as much, if not more affected than any other, unless it be the postero-external. It has been pointed out that in the other cases this group shows practically no change.

In the cervical and lumbar enlargements there is also very considerable decrease in the fibres composing the network of the anterior horns, especially in the central portion. This change, which does not occur in the dorsal region, causes a very obvious pallor of the sections stained by Weigert's method.

The posterior horns, the cells and reticulum of Clarke's column, and the other portions of the gray matter, appear perfectly normal in all regions of the cord.

White matter.—In all the sections examined there is a slight general increase of the interstitial tissue; this is greatest towards the periphery of the cord, and in the neighbourhood of large fissures and vessels; the adventitia of the latter is also very much increased. In no instance do the nerve-fibres appear to be diminished in number, and there is no indication whatever of any tract degeneration. We think that the slight general interstitial overgrowth which is present is probably not unlike the fibrotic condition occurring in many organs as a result of old age; such a condition is not at all uncommon in the spinal cords of old people.

Anterior Roots.—The anterior nerve roots in the cervical and lumbar regions are much atrophied.

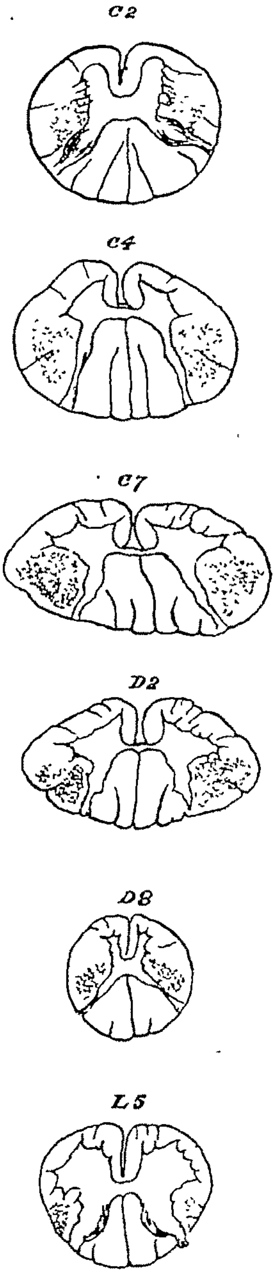
Vessels.—Most of the small and medium-sized vessels are in the condition described by Gull and Sutton of arterio-capillary-fibrosis; those of the peripheral nerves and skin also show the same change.

The *membranes* are not thickened, and appear fairly normal.

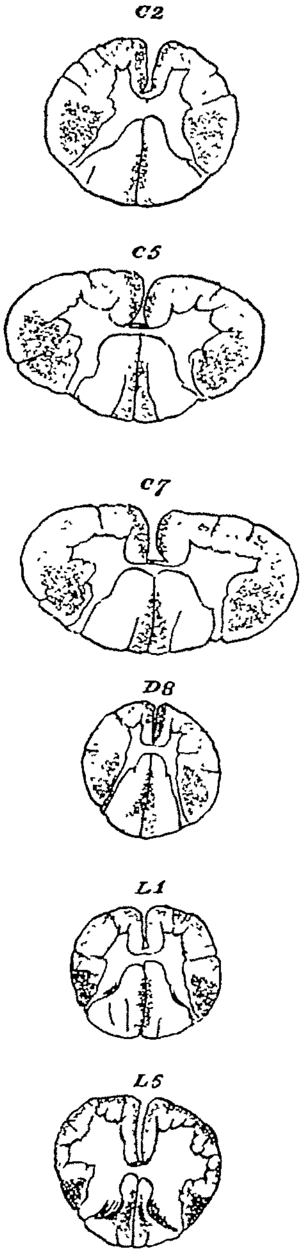
Spinal ganglia.—Several were examined from the lumbo-sacral enlargement. Marchi sections show no fatty degeneration, but the cells contain an abundance of black pigment in small granules. Nissl-stained sections show that many of the cells are somewhat shrunken and shrivelled, and the pigment in these sections is yellow in colour. There is, however, no very definite degeneration, and nothing of an acute nature. There is a slight increase of the fibrous tissue throughout the ganglia.

Peripheral nerves.—The right and left great sciatic and ulna nerves were examined in longitudinal and transverse

PLATE I.



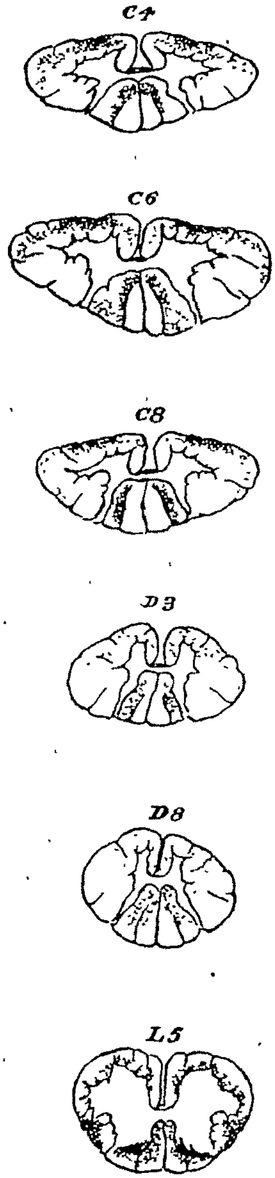
Case No. 1.



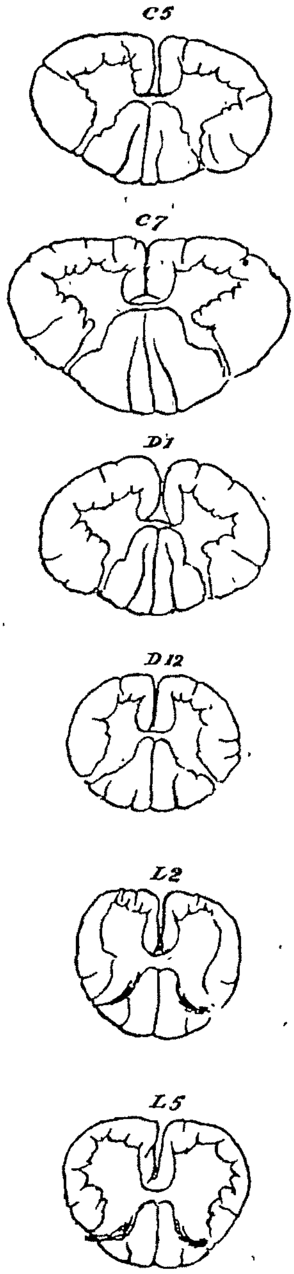
A. F. Tredgold, del.

Case No. 2.

PLATE II.



Case No. 3.



A. F. Tredgold, del.

Case No. 4.

sections. In the Marchi preparations there appears to be considerable diminution in the number of fibres, but there is no recent degeneration. In sections stained by the carmine-Weigert method it is readily seen that there is a considerable deficiency in the number of fibres. In the transections of some of the bundles there are quite large areas, as much as one quarter of the section, almost entirely devoid of nerve-fibres, their place being taken by an overgrowth of connective tissue.

Thumb muscle.—A section of this stained by Marchi's fluid, shows that there are a few fibres in which striation is well marked, and which appear to be quite healthy; but a still larger number are cloudy looking, and their striation is indistinct, although they do not show any fatty change; others, however, are in a typical condition of fatty degeneration.

We have considered it advisable to include this case, since the microscopical appearances almost exactly agree with those in the three preceding ones; the cells and fibres undergo exactly the same chronic atrophy, there is just the same increase of pigment, and just the same thickening and fibrosis of the vessel walls. In one respect there is a difference; it has been seen that in the other three cases the mesial-anterior group of cells in the anterior horns is comparatively little affected, the chief change being in the lateral groups; in this case, however, there are as many atrophied cells in this group as in any other. We are unable to say whether the change in the anterior horn cells is primary or secondary to the joint change, or to give any satisfactory explanation of this difference, we simply record the fact.

REMARKS.

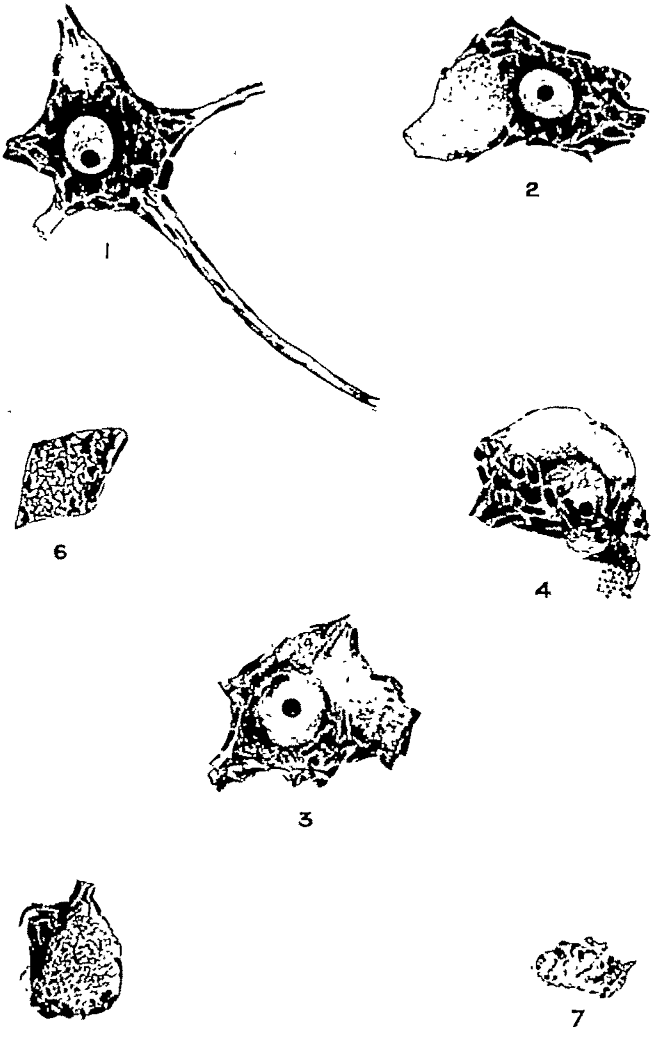
Degeneration of the motor tract is the anatomical lesion present in several diseases having distinct clinical features. Thus it occurs in Friedreich's disease, in combined lateral and posterior sclerosis, and in general paralysis; but in these other neuronic systems are also affected. Degeneration of the motor path may also be the result of a local lesion, *e.g.*, anterior polio-myelitis, polio-encephalitis, embolus, &c.; and lastly, cases exist in which not a degeneration, but an arrest of the development of the efferent tract occurs, apparently due to a simple agenesis; these cases are usually associated with microcephaly.

On the other hand, there are instances in which the motor tract undergoes a *primary degeneration*, neither the result of a localised lesion nor part of a more general disease; clinically this may appear as amyotrophic lateral sclerosis, progessive muscular atrophy, primary spastic paraplegia, or bulbar paralysis. It is with such primary degeneration that the present paper deals, it must, however, be remarked that as the *result* of the change in the motor path, other conducting tracts may be affected.

(I.)—*The Nature of the Morbid Process.*

There is every reason for considering the change in these cases to be a subacute or chronic degeneration of a portion or the whole of the motor tract, that is, of the upper segment alone, of the lower segment alone, or of both segments together. The cases which have just been described in detail demonstrate that the change is a slow decay of individual neurones. In no instance could we find any evidence of acute change in the cells, and it may be remarked that also in the nerve-fibres and in the muscles the process is usually one of gradual atrophy, with very little appearance of true fatty degeneration like that met with in acute processes. The cells become shrunken and irregular in outline; the Nissl bodies gradually disappear, their place being taken by a large collection of yellow pigment which stains black with Marchi's fluid; the nucleus becomes smaller and its outline indistinct, later it is displaced to the periphery of the cell, and at last disappears; the processes get much thinner and eventually break off; and finally a small mass of granular pigment is all that is left. These successive changes are shown in Plate III. which is drawn from cells stained by Nissl's method. The nerve-fibres and their end-organs, the muscle fibres, wither away in the same manner; in the muscles a true fatty degeneration does in some instances occur, and fibrils may be seen in

PLATE III.



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Showing the stages of degeneration of an anterior horn cell.

To face page 486.

this condition, but very often the individual fibres gradually become thinner, their striation disappears, and they are finally replaced by connective tissue. In longitudinal sections of the peripheral nerves we have at times come across small portions of naked axis cylinders; in transverse sections the diminution in the number of fibres, and increase in the connective tissue is particularly well seen. Neuroglia gradually takes the place of the atrophied nerve-fibres in the central nervous system, causing a sclerosis which is secondary and not primary.

The process is therefore slow, but progressive, and the best explanation which can be offered of its occurrence is that the neuron has reached that stage at which its inherited vitality is exhausted, and it is no longer capable of performing the metabolism necessary to its life. The presence of intracellular pigment which is almost universal in these cases is probably an indication of presenile decay. Various theories have been put forward to otherwise explain the condition, thus by some it has been thought to be due to a toxic influence, but although there can be no doubt that certain poisons have a selective action upon certain neuronic systems, there does not appear to be any evidence in support of this view in these cases; the changes in the cells are entirely unlike any toxic condition with which we are acquainted. Neither can vascular alterations be looked upon as the primary cause of the disease; it is true that in a very large proportion of these cases structural changes in the vessel walls are found (arterio-capillary-fibrosis), but these vascular changes are present throughout the entire nervous system, and in many cases other parts of the body also, so that it is unlikely that the degeneration would be confined to the efferent tract unless there existed a tendency to premature decay on the part of its neurons. It is possible, however, that the vascular alterations, by bringing about an inadequacy of the circulation, may act as a contributory factor. The age at which these diseases begin (a time when the motor system is usually in full vigour) and the fact that several members of a family may be similarly affected, lend considerable support to the view of hereditary influences. It may be asked: Is the degeneration of a particular system of neurons entirely due to these tendencies, or may the site of the disease not be determined by some external cause? It has been repeatedly pointed out by one of us that in tabes, for example, the initial site may be brought about by occupation, &c.; thus, in those whose work entails constant stress upon the lumbo-sacral region of the cord, this is the part first affected, whilst in others in whom the arms are chiefly used, the disease begins in the upper part of the cord.* It is therefore likely that in the cases we are now considering the occupation of the patient may determine which *portion* of the efferent tract will be first affected, but there does not seem to be any reason for thinking that the selection of the *tract* itself (whether afferent or efferent) can be so influenced; such must be due to hereditary predisposition. It should be remembered that excessive motor sense impressions are but the outcome of excessive movements, and that the one is commensurate with the other; the stress on both systems is therefore equal.

With regard to the morbid anatomy of these diseases (especially amyotrophic lateral sclerosis), it has been frequently noticed that in some instances the sclerosis in the pyramidal tracts cannot be traced higher than the medulla or pons, in others as far as the crura, and in others up to the internal capsule, although most observers have been able to find evidence of change, in the presence of granular bodies, as high as the motor cortex. There are, of course, many difficulties in the way of demonstrating sclerosis higher than the capsule, but even allowing for this there can be no doubt that it is frequently more pronounced in the most distant part of the efferent tract. The explanation of this is easier if we remember that the change is not an acute one like that resulting from a focal lesion, but that a slow and gradual death takes place, the parts most distant from the cell being the first affected.

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* The cab-driver would use his legs but little, his arms and hands a great deal in driving and lifting the boxes on and off his cab, hence the limitation of the disease in Case 8. Two other examples occurred in the practice of one of us (F. W. M.). A cooper, who wielded a 4 lb. hammer, was affected first in the right arm with amyotrophic lateral sclerosis; but an Italian waiter was affected first and most severely in the muscles of the left hand and shoulder; upon being asked whether he could in any way account for this, he said he carried a tray all day long with his left hand. The familiar figure of the waiter of the Italian restaurant with the loaded tray poised on the left hand, level with the shoulder, suggests stress on the very muscles which were first affected in this man.

We may here describe a case which affords a microscopical demonstration of this point:—The patient had well-marked hemiplegia and aphasia, due to thrombosis of the left middle cerebral artery, death taking place on the twelfth day. The cells of the cortex were stained by Nissl's method, but after examining many sections it was found to be quite impossible to distinguish between those of the two hemispheres, that is to say, no departure from the normal could be detected in the pyramidal or other cells of the left motor region, although the patient was quite hemiplegic. On examining the pons and medulla there were found to be definite alterations in the efferent tract. At this level there was little (scarcely any) Marchi degeneration (what was present was confined to small fibres, possibly collaterals, and therefore almost terminal ones); many of the large fibres, however, were greatly swollen, and appeared to be in a condition of coagulation necrosis. There were no similar fibres in the corresponding region of the other side. Still lower down, in the cervical cord, many fibres were seen in a typical condition of fatty degeneration in the left direct and right crossed pyramidal tracts. Thus it is seen that in these cases of gradual death of the neuron, degeneration *simultaneously throughout the course of the fibre does not take place;* the fatty change begins in the most distant part of the fibre, and then ascends towards the cell; this fatty change being preceded by a swollen condition of the axone.

This case affords an explanation of the peculiar microscopical appearances which have been observed in amyotrophic lateral sclerosis, and why it is that although degenerative changes are always well marked in the distant portions of the tract, they become less evident in the higher regions. Occasionally, if the case is of considerable standing, definite degeneration may be found in the motor cortical cells, as in Case No. 1.

Marie drew attention to the fact that in cases of amyotrophy emotional disturbances frequently exist. Our own experience entirely confirms this, the patients very generally showing a ready tendency to burst into tears, or, less often, into laughter, for slight causes. There is psychomotor slowness in the emission of ideas, the memory and attention are not lost, but dormant, and require an effort to be revived. There is no true dementia, however, and this is in accordance with the fact that in the cortex the degeneration is confined to the large Betz cells; *the smaller and medium-sized pyramids and the layers of tangential and superradial fibres being quite unaffected.* This constitutes a very important microscopical difference between this condition and those of general paralysis and senile dementia associated with degeneration in the efferent tract. Sometimes in amyotrophy a slight thickening and opacity of the pia-arachnoid membrane over the motor cortex may be found, which, in view of the limitation of the degeneration, must certainly be looked upon as secondary. Pierret considers that there is a close relationship between general paralysis and amyotrophic lateral sclerosis.

(II.).—*The Pathological Relation between the Upper and Lower Motor Segments.*

Charcot maintained that in cases of amyotrophic lateral sclerosis, the primary lesion was a degeneration of the pyramidal tracts, and that this caused a "deuteropathic" affection of the ganglion cells of the anterior horns. Sir Wm. Gowers and Leyden strongly object to this view, and consider that a primary and independent degeneration takes place throughout both the upper and lower segments, the change in one not being brought about by that in the other, but both being due to a common cause; indeed, they consider that in by far the larger number of cases, both segments are affected simultaneously, and that it is extremely rare to find, in cases of progressive muscular atrophy, an absence of change in the pyramidal tracts also.

In support of Charcot's view, it must be admitted that a degeneration of the pyramidal tracts resulting, say, from a cortical lesion, may be followed by changes in the anterior horn-cells. Schäffer, in a case of cerebral hemiplegia of short duration, found chromolytic changes in the postero-external group of anterior horn cells, which he regarded as secondary to the degeneration of the pyramidal tracts. Marie thinks that diminution in the size of the anterior horn is almost always present in long-standing cases of degeneration of the pyramidal tract. Fürstner and Knoblauch also noted the same thing, and pointed out that it was the lateral cell groups which were chiefly affected.

The different kinds of birth palsies also show that degeneration or arrest of development of the upper efferent tract may bring about very important changes in the cells and fibres of the lower tract. In a recent article we described three such cases of primary cerebral lesion, and in each of them, in addition to the atrophy of the corresponding pyramidal tract, there was marked diminution in the anterior horn cells of the arm and leg enlargements, and atrophy of the peripheral nerves and muscles.

One also at times sees in cases of hemiplegia occurring in middle age a very considerable wasting and flaccidity of the muscles which are rendered paralysed. A large part of such may very probably be the result of disuse, but in some cases this explanation seems by no means adequate and in these it almost looks as if the upper segment did really exercise a kind of trophic influence over the lower. It must be admitted that this only takes place after the lapse of some considerable time; the subject is, however, one well worthy of further attention. There can be no doubt that the *afferent* fibres exert a trophic action upon the anterior horn cells. Warrington found chromolytic changes in certain of these cell groups after section of the posterior roots, which he attributed to the withdrawal of afferent impulses normally acting upon these cells in the production of reflex spinal tonus.

Whilst therefore there can be no doubt of the existence of a trophic action between the upper and lower parts of the efferent tract in some cases, the presence of degeneration in one portion resulting from degeneration in the other seems to be rather the exception than the rule, and it is now well established that disease may involve either segment separately, or both together. In Case No. 4, although the condition is perhaps not strictly a primary degeneration of the lower segment, the change is confined to that segment, and in spite of its duration of several years there is no evidence of implication of the upper portion of the tract. There have also been a few cases recorded (by Strumpell and others) of the opposite condition, the degeneration being limited to the pyramidal bundles and the anterior horns showing no change (primary spastic paraplegia). One also not infrequently meets with similar cases of a temporary nature, in which spastic paraplegia is present, the patellar reflexes being greatly exaggerated, as a rule recovery takes place after a longer or shorter time, and hysteria is often invoked as the cause; but many such cases may be directly traced to an infectious process, such as influenza, &c. On the other hand there are certain poisons, of which diphtheria is a well-known example, which seem to have a special predilection for the lower segment. If, therefore, each segment of the motor tract is specially susceptible to the influence of particular poisons, it seems legitimate to conclude that there also may be different hereditary tendencies present in the two tracts. In some persons there may be a tendency to premature decay in the upper portion, in others in the lower portion, and still in others throughout the entire motor system.

(III.)—*The Involvement of other Neuronic Systems.*

Many writers would exclude from the cases we are now considering those in which other tracts than the efferent are affected; but although we most certainly hold to the view that a degeneration in the motor system is the primary and essential change, and that in many cases no other tracts are affected, it is certain that in a not inconsiderable number of cases (amyotrophic lateral sclerosis in particular) atrophic changes also exist in other tracts of the white matter. Such changes, however, are to be looked upon rather as secondary in nature than as a true primary degeneration like that occurring in the pyramidal tracts. These secondary changes take place in two distinct systems—*i.e.*, association and afferent.

Association fibres.—As is well known, the anterior horn-cells of different segments of the spinal cord are brought into communication with one another by means of short and long association systems. Many of the short fibres probably do not leave the gray matter, but the longer ones occupy the antero-lateral columns lying intermediate between the periphery of the cord and the gray matter of the horns. In many cases of amyotrophic lateral sclerosis and of progressive muscular atrophy a well-marked band of interstitial sclerosis is to be seen in this region, indicating the involvement of these fibres. Osler also mentions a case in which sclerosis occurred in the medial longitudinal bundles, which are generally thought to convey association fibres from the cord to the medulla and pons. It is likely that the very great disappearance of fibres from the network of the anterior horns is partly due to atrophy of short association fibres; it certainly cannot be entirely due to affection of the terminal filaments of the pyramidal tracts as might be supposed, because in Case 4 the diminution in this network is almost as marked as in the other cases, and yet in this the upper efferent tract was not involved. These association systems are evidently part of the *lower* motor segment; they undergo no change if the degeneration is confined to the upper segment (as in hemiplegia, &c.), and their atrophy appears to be proportional to the number of anterior horn-cells affected; possibly it is of a secondary nature, and due to the fact that they are put out of action by the death of the anterior horn-cells, which they usually serve to connect. According to the view of von Monakow, which is supported by Schäfer's experimental operations, the terminal arborisation of the pyramidal systems does not come into direct connection with the dendrons of the spinal motor neurons, but through the intervention of intercalary neurons of the second type of Golgi.

The opposite halves of the cord are similarly connected by fibres passing through the anterior commissure, and in most cases there is a very well-marked sclerosis in this region also.

Afferent fibres.—Charcot, Pierre Marie, and other observers have drawn attention to the fact that in amyotrophic lateral sclerosis the *posterior* columns are frequently sclerosed, and although this has been denied by other writers, our experience certainly confirms it. The extent of this change in our cases will readily be seen by a reference to Plates I. and II., and to the description of the cases. We were also able to demonstrate atrophy of some of the fibres of the posterior roots. It must therefore be admitted that changes do occur in the afferent tracts; the explanation, however, is not easy, and there seems to be no recorded instance of atrophy of any other portion of the afferent system than the posterior columns. All writers agree that the cells and reticulum of Clarke's column, the direct cerebellar and the ascending tracts in the antero-lateral column are unaffected. We suggest the following explanation of this atrophy of posterior column fibres. These fibres convey impressions arising in the deep structures, especially the muscles; in support of this statement we may refer to Sherrington's important observation that one-third to one-half the fibres entering muscles are afferent. It is highly probable that other sensory impressions (tactile, pain, and temperature) which come from end organs situated in the skin and subcutaneous tissues are conducted by the short fibres which enter the gray matter of the cord immediately, terminating in an arborisation around cells of the substantia gelatinosa of the posterior horn. In degenerations of the motor tract, although the muscles are profoundly atrophied and in many cases converted into little more than fibrous tissue, the overlying skin remains unaffected, and the ordinary sensations are not interfered with; it therefore seems possible to look upon the change in the posterior columns as being due to the secondary disuse atrophy of fibres coming from the muscles. We know that similar changes take place in *all* the afferent tracts after amputation of a limb; we have ourselves observed this in several such cases, and this view explains why, in wasting of the muscles only, such change should be confined to the posterior columns.

In addition to these secondary alterations in tracts, some cases, especially those of long duration, show a diffuse increase in the interstitial tissue throughout the cord, the septa and adventitia of the blood-vessels being also much thickened. It is not uncommon to find this condition in other cases of chronic nervous degeneration, and also in old age.

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ON THE PALLIO-TECTAL OR CORTICO-MESENCEPHALIC SYSTEM OF FIBRES.

BY CHARLES E. BEEVOR, M.D., F.R.C.P.,
AND
SIR VICTOR HORSLEY, F.R.S., F.R.C.S.

(*From the Laboratory of Chemical Pathology, University College, London.*)

INTRODUCTION AND METHOD.

IN the course of an investigation of the fibres composing the crus cerebri in a number of animals (twenty cats, eleven monkeys, one dog, and two badgers) localised lesions in the pallium or cortex cerebri had been made by one of us (V. H.). While tracing the degenerations which resulted from such lesions we have specially followed out the connections which have for some years been known to exist between the cortex cerebri and the mesencephalon. In all cases the procedure was the same. A small area of the cortex in an animal anæsthetised with ether or chloroform was either excised or separated by a tangentially-directed incision through the corona radiata, so as to undermine the part determined upon.

Antiseptic precautions were always taken, and at the end of three weeks the animal was chloroformed, bled to death, and the vessels were washed out with Muller's fluid. The whole encephalon when fixed was cut into slabs, stained by Busch's modification of the Marchi method, and cut in serial sections. Only cases of healing by immediate union were accepted.

HISTORY.

The former investigations on this question may be grouped chronologically as follows:—

In 1891 the pathological observations of Zacher[1] on man,

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[1] *Archiv. fur Psych.*, Bd. xxii., 1891, p. 654.

though necessarily indeterminate owing to the length of time elapsing between the occurrence of the lesion and the death of the patient, appeared to indicate that fibres pass from the occipital cortex to the mesencephalon by the lateral segment of the cerebral peduncle. His cases also suggest that the corpus geniculatum internum and the inferior corpus quadrigeminum were in connection by fibres with the cortex, and possibly with that of the temporal lobe.

In 1895 Edinger[1] first proved by the degeneration method in the bird the occurrence of an occipito-mesencephalic tract. The fibres proceeding from the occipital pole of the bird's hemisphere pass dorsally to the basal-frontal bundle and end in the deepest layers of the mesencephalon. The lesion was an extirpation of the "occipital" pole, and it extended forward to involve slightly the posterior part of the basal ganglia.

In the same year (1895) Boyce[2] showed that after removal in the cat of the anterior third of one cerebral hemisphere there was in the middle region of the optic thalamus a group of scattered large degenerate fibres leaving the internal capsule and entering the optic thalamus, where they were grouped around the lower and inner aspect of the ventral lateral geniculate body. In more posteriorly-made sections they passed backward beneath the pulvinar and came to the surface as a well-marked group immediately external to the anterior corpus quadrigeminum. Some of these fibres entered the base of the corpus on the same side as the lesion, and probably some fibres terminated here; others he observed to cross over in the roof of the aqueduct to the opposite side, where they possibly terminated in either of the corpora quadrigemina. Fibres could also be traced back to the quadrigeminal region, being given off from the degenerate fibres in the capsule during their course to form the crusta. One well-marked bundle passed from the upper and incurved extremity of the pyramid just before the crusta is formed to the roof of the aqueduct, and lower down isolated fibres came off from the outer and upper extremity of the crusta and curved round to the quadrigeminal region. Small groups of fibres left the dorsal and inner portion of the pes pedunculi and passed back to the tegmental commissural region of the same side, but whether they actually crossed over in the posterior commissure to the opposite side was not proved.

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[1] "Ueber die Entwickelung des Rindensehens," *Archiv. für Psych.*, Bd. xxvii., 1895, p. 950.

[2] *Phil. Trans. Roy. Soc.*, vol. 188, Series B, 1895, p. 335.

Lower down also he found that degenerated fibres left the crusta and passed back to the quadrigeminal region of the same side.

According to Dejerine[1] the radiations of the anterior corpus quadrigeminum, *i.e.*, tecto-pallial fibres, pass above and in front of the corpus geniculatum externum which they separate from the posterior segment of the internal capsule, and particularly from the bundle of Turck in front of the corpus geniculatum internum, and between this last and the pulvinar. Then they become superficial while running together to form the brachium of the anterior corpus quadrigeminum, and they spread out finally into the superficial and middle layers of the anterior corpus quadrigeminum.

Simpson,[2] in 1901, observed fibres in several cats in which "an attempt was made to divide the projection fibres arising from the left motor cortex in its whole extent." He observed fibres from the posterior aspect of the crusta passing back through the tegmentum and ending in the homolateral superior colliculus,[3] a few crossing to the contra-lateral colliculus, while in addition a fine degeneration was also observed in the locus niger. In the dog and monkey he found no such fibres.

Results of the Present Research.

(1) *General Statement.*

As the present research is founded chiefly on observations on the cat as representing the carnivora, and the macacque monkey (usually *Macacus rhesus* and more rarely *Macacus*

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[1] "Anatómie des Centres Nerveux," Tome ii., Fasciculus 1, 1901, p. 70.

[2] *Journal of Physiology*, vol. xxvii., 1901, p. 11.

[3] The terms superior and inferior colliculus instead respectively of anterior and posterior corpus quadrigeminum, though not in general use, appear to deserve general adoption as being more succinct.

sinicus) as representing the Primates, it will be understood that a general statement is only completely applicable to the higher of these animals, in which there is a well-developed non-excitable area (frontal) in front of the so-called motor or excitable cortex. With this proviso the general scheme of a pallio-tectal system may be stated as follows :—

From the frontal cortex no fibres could be traced by us to the mesencephalon ; from the temporo-sphenoidal cortex very few fibres; while from the occipital lobe a fair number, and from the excitable cortex a large number of fibres can be followed to the corpora quadrigemina and mesencephalon.

The course taken by the different groups of fibres may now be detailed, and as the occipito-mesencephalic group is somewhat special by reason of the highly-developed visual association between the cortex of the cuneal region and the superior colliculus (anterior corpus quadrigeminum) we will describe that first.

(1) *Occipito-Mesencephalic Fibres.*

The results we have obtained from the occipital lobe are strikingly concordant and fully confirm Edinger's original generalisations on this subject.

In proportion as more of the area of cortex containing Gennari's[1] streak is involved in the lesion the number of degenerated fibres passing to the colliculus increases.

The occipital lesions produced in the present investigation were all situated on the outer surface of the pallium.

In one observation in the monkey we made a small lesion involving the posterior lip of the "affen-spalte," to which Gennari's streak reaches in *Macacus rhesus*. From even this small lesion, some fibres passed to the anterior colliculus, showing how complete the association between the occipital area and the mesencephalon is.

The fibres which descend from the occipital cortex to the superior colliculus are large and stand out distinctly from the medium-sized occipito-thalamic and occipito-geniculate fibres and from the small callosal fibres and fine collaterals which enter the corona radiata in large numbers. Some of the occipito-tectal fibres pass among the fibres composing Gratiolet's radiation, others run through the mesial region of the inferior longitudinal bundle (posterior fourth). This is in harmony with the converse observations of Schütz, made on microgyric brains, in which fibres of the inferior longitudinal bundle were found to be really tecto-occipital in character.

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[1] The comparative morphological topography of Gennari's streak is not yet worked out, but we have accumulated a large mass of material on which the statement above is based.

In traversing the thalamus the occipito-mesencephalic fibres run for the most part in the stratum zonale, but also partly through the lateral part of the dorsal nucleus.

A very few pass just mesially to the corpus geniculatum internum, and all are distributed to the whole breadth of stratum griseum profundum of the anterior colliculus.

(2) *Temporo-Mesencephalic Fibres.*

It will be better to divide the results from lesions of the temporal lobe, according to the animals, cat and monkey, operated on, because the homologies of the gyri in two so distant genera have not yet been accurately determined.

(*a*) Cat.—The terminology descriptive of the temporal gyri in the cat is best given in Flatau and Jacobsohn's[1] handbook. We have made lesions in the small gyrus behind the Sylvian fissure, *i.e.*, the gyrus Sylviacus posterior and in the next gyrus behind it, viz , the gyrus ecto-Sylvius posterior. Of these two, injury of the former only reveals fibres passing to the locus niger. Lesion of the posterior limb of the ecto-Sylvian gyrus demonstrated an outflow of the fibres both large and small passing to the mesial side of the posterior extremity of the lenticular nucleus entering the outermost bundles of the internal capsule, and thence distributed to (*a*) the optic thalamus, (*b*) the corpus geniculatum internum, (*c*) the posterior brachium of the corpora quadrigemina (colliculi), (*d*) the pontine nucleus. Of these it is to be noted that a number of fibres in the posterior brachium turn up towards the posterior colliculus, but we have never been able to follow them into that ganglion; that

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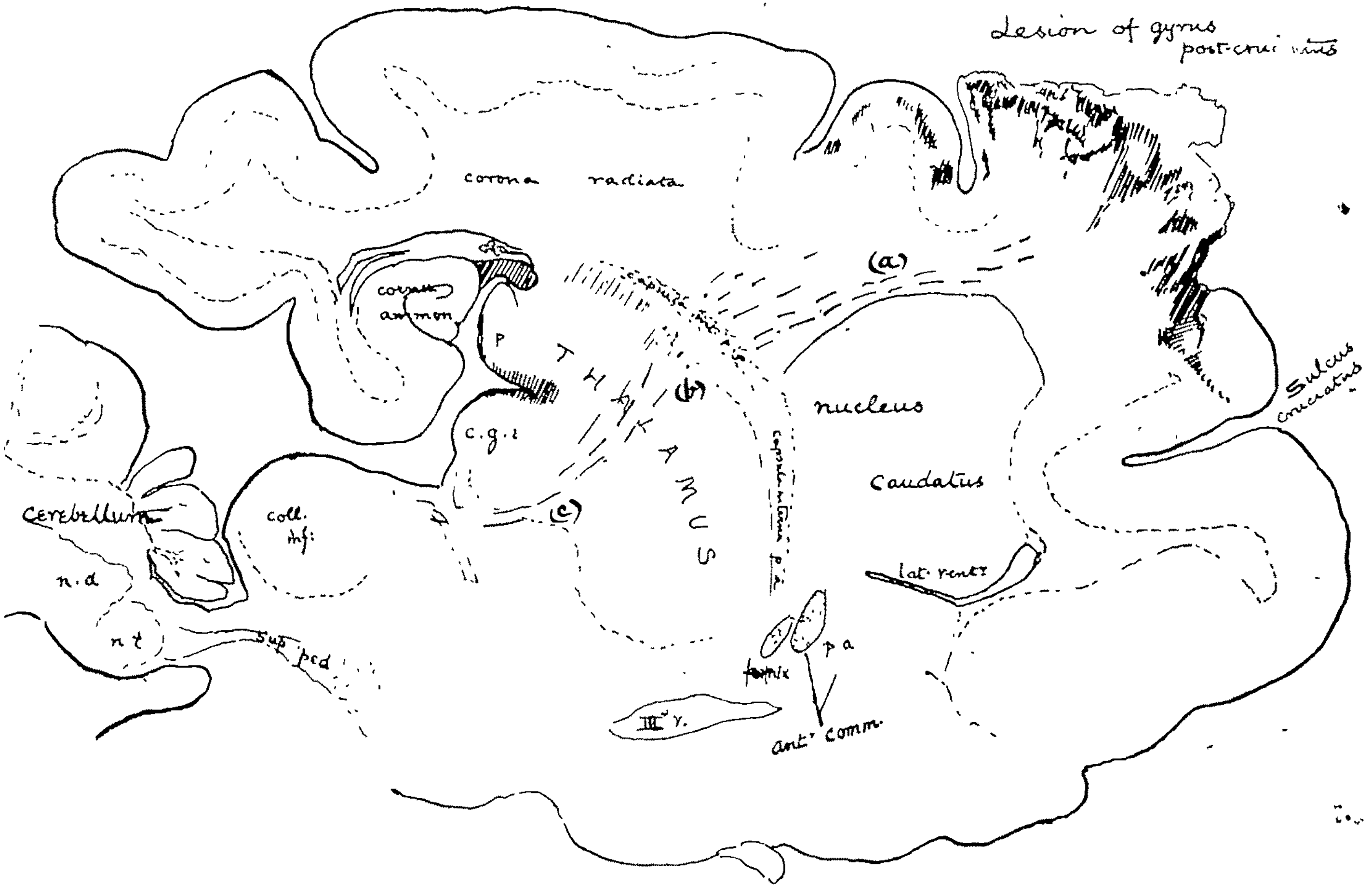
[1] "Handbuch der Anatomie und Vergleichenden Anatomie des Centralnervensytems der Saugethiere." 1899.

FIG 1

Pallio-tectal fibres from localised lesion of parietal cortex Sagittal section at 45° to the vertical plane. Cat. Marchi prepn.



(a) Pallio-tectal fibres in corona radiata passing back to cross the posterior limb of the internal capsule.
(b) Do. traversing lattice layer and lateral nucleus of thalamus.
(c) Do. curving mesially to corpus geniculatum internum to enter the superior colliculus and [illegible]

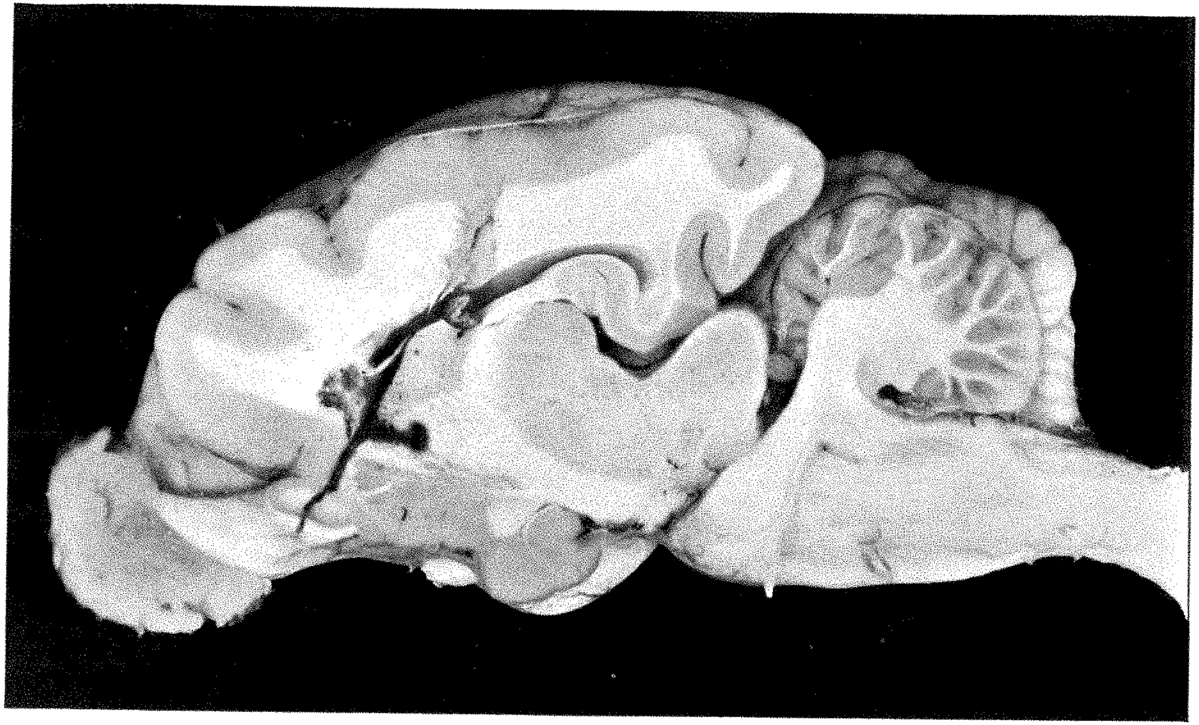
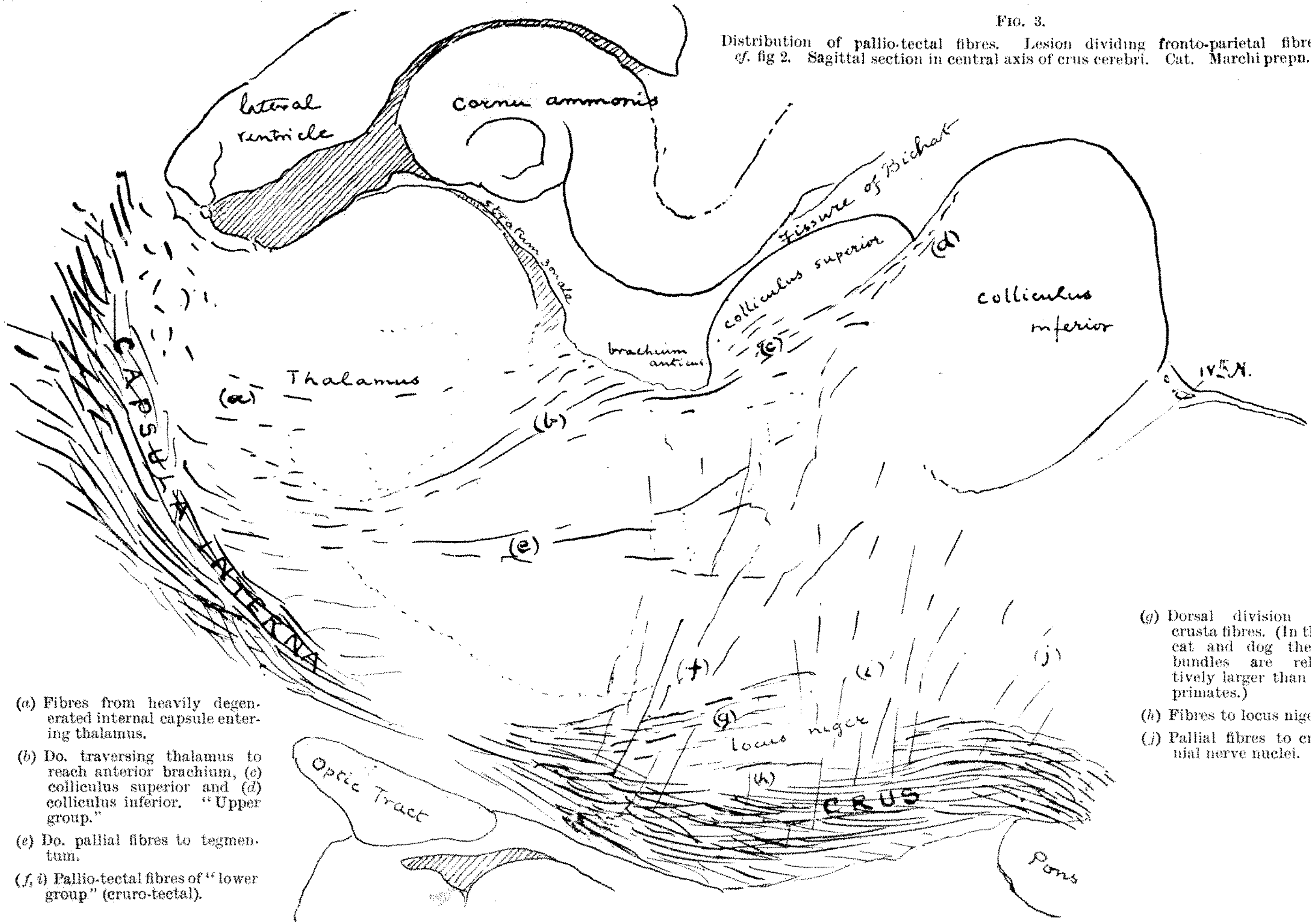


FIG. 3.

Distribution of pallio-tectal fibres. Lesion dividing fronto-parietal fibres, *cf.* fig 2. Sagittal section in central axis of crus cerebri. Cat. Marchi prepn.



(*a*) Fibres from heavily degenerated internal capsule entering thalamus.

(*b*) Do. traversing thalamus to reach anterior brachium, (*c*) colliculus superior and (*d*) colliculus inferior. "Upper group."

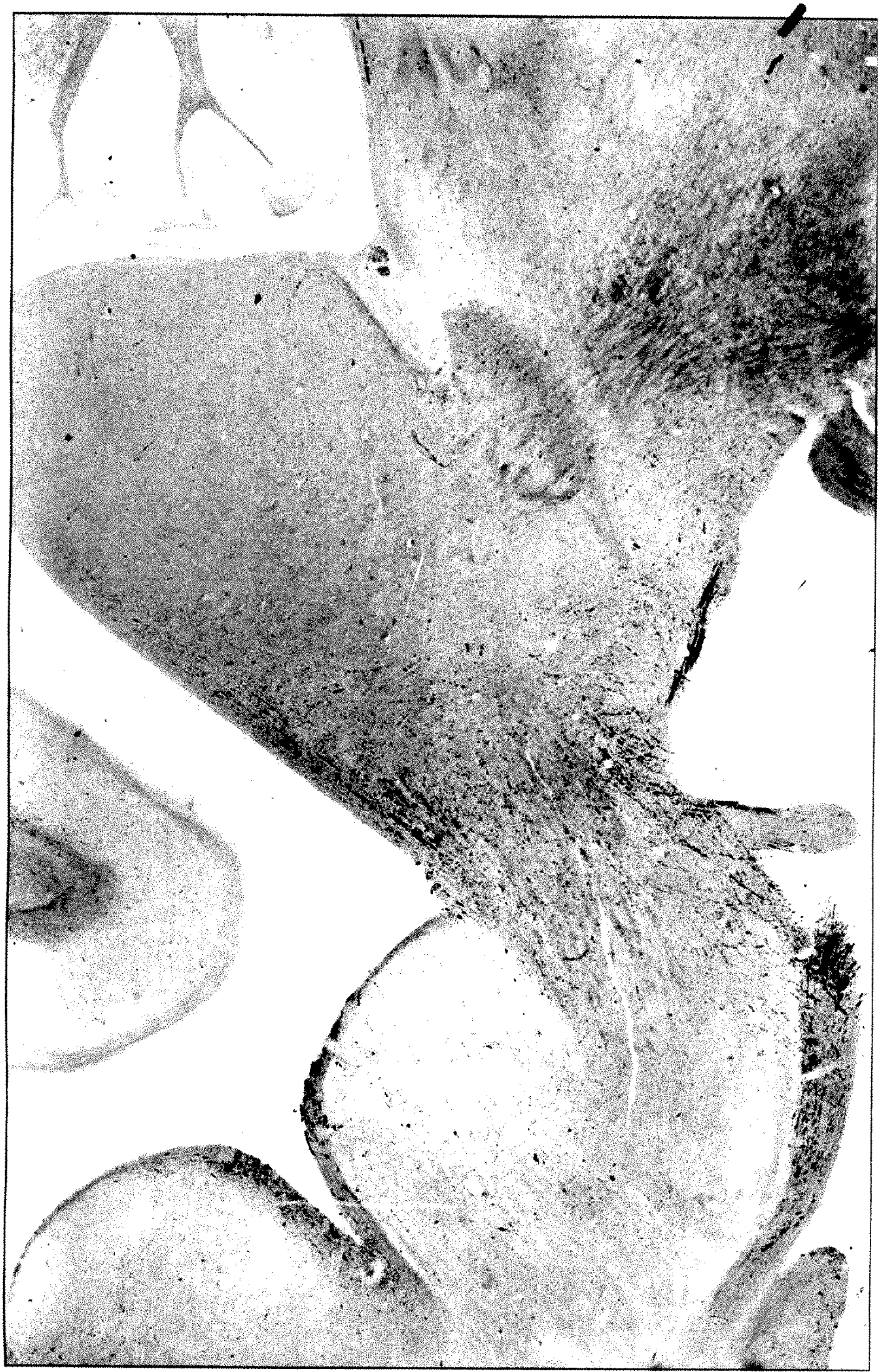
(*e*) Do. pallial fibres to tegmentum.

(*f*, *i*) Pallio-tectal fibres of "lower group" (cruro-tectal).

(*g*) Dorsal division of crusta fibres. (In the cat and dog these bundles are relatively larger than in primates.)

(*h*) Fibres to locus niger.

(*j*) Pallial fibres to cranial nerve nuclei.



is, we have never been able to follow them beyond the gray matter forming the anterior fused border of the nucleus of the lateral fillet. The fibres which pass to the brachium are accompanied in the first part of their course by the fibres to the internal geniculate body. The fibres to the pons run down on the outside of the crus as Dejerine[1] has shown in man, and terminate in the upper and outer part of the frontal extremity of the pontine nucleus. In this animal (cat) they cannot be traced for a greater distance than one-third of the antero-posterior length of the pons.

(*b*) Monkey (*Macacus rhesus*).—Of the lesions which we made in the temporal gyri, all involved the posterior half of the gyrus operated upon.

In all cases fibres were traced to (*a*) the thalamus opticus, (*b*) the corpus geniculatum internum, (*c*) the posterior brachium, and (*d*) the locus niger. These fibres for the most part are of fine or medium size, and they appear to be coarser in proportion as they arise from cortex which was nearer to the Sylvian fissure.

(3) *Parieto-Mesencephalic and Combined Fronto- and Parieto-Mesencephalic Fibres.*

The fibres coming from the excitable cortex we have investigated in two ways, either by producing a small lesion in a localised area of the so-called motor region, or by division of the corona radiata so as to undermine selected gyri, or by an extensive incision which was carried vertically through the hemisphere so as to separate the anterior third or half more or less completely.

The results of these experiments will best be described as before, under the denomination of the animal investigated.

(*a*) Monkey.—In this animal the system of fibres connecting the excitable area with the mesencephalon is relatively only moderately developed, and was not in fact observed by Simpson in the two animals which he examined.

Lesions.—In two monkeys (*Macacus sinicus* and *Macacus rhesus*) we made a horizontal incision through the hemisphere in the plane of the anterior end of the intraparietal sulcus so as to cut off the fibres descending from the two central gyri. In a third animal (*Macacus rhesus*) we made a vertical stab incision beneath the whole length of the ascending parietal gyrus and continued beneath the two upper temporal gyri. In the two first cases fibres were traced to the thalamus opticus, but in one of them only could fibres be followed to the posterior brachium. In the third case, besides the fibres passing to the thalamus, others pass through the middle of the thalamus, some even entering the posterior commissure, while others were followed into the posterior brachium (probably temporo-mesencephalic fibres). A second group of fibres arise from the outer part of the crus and pass through the locus niger to ascend towards the tectum.

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[1] "Anatomie des centres nerveux," Tome 2, Fascic. 1, p. 145.

(*b*) Carnivora.—In three cats, one dog, and one badger, we made a strictly limited lesion in the post-crucial gyrus. In the one experiment on the dog we observed no fibres passing to the tectum (*cf.* Simpson *loc. cit.*), but this is only a single observation, and we do not therefore regard the question of their presence or absence in the dog as settled. In the cat and the badger a well-marked system of pallio-mesencephalic fibres exists. The fibres, for the most part large, leave the pyramidal tract in two definite groups, which we may speak of as upper and lower respectively.

The upper group of fibres, which are apparently those previously seen by Boyce, leave the internal capsule at about the junction of its outer and middle thirds, as seen in horizontal section; they pass backwards through the thalamus to the inner side of the corpus geniculatum internum, partly enter the anterior colliculus, and partly pass beneath it to the posterior colliculus; some of these fibres seem to terminate in the thalamus.

The lower group, which we think might conveniently be also called the cruro-tectal group, arise from the crus cerebri at points all along the outer one-third of its dorsal surface, and the more anterior of these pass inwards and terminate in the anterior colliculus and locus niger,[1] while the more posterior pass upwards and backwards to gain the posterior colliculus. Many of these latter run in the inferior brachium. These fibres to the posterior colliculus terminate in the anterior half of the large ovoid nucleus of that body.

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[1] Probably these are the fibres traced by Sherrington and others as connecting the crus and locus niger.

A few of the outermost fibres turn down from among those which pass beneath the superior colliculus and run in or with the tractus transversus peduncularis.

Combined Frontal and Parieto-Mesencephalic Fibres.

In four cats we separated the whole fronto-parietal region of the hemisphere by an incision which passed through the junction of the anterior and middle thirds of the hemisphere.

The effect of this large division of the corona radiata was to increase the number of degenerated pallio-mesencephalic fibres, as well as to cause degeneration of large numbers of fibres terminating in the thalamus opticus. These latter observations, therefore, are confirmatory of the fact that the so-called motor region is in close association with the anterior colliculus.

(4) *Fronto-Mesencephalic Fibres.*

To examine the important question whether the frontal region, *i.e.*, the area of cortex in front of the excitable cortex, sends any fibres to the mesencephalon we have made limited lesions of the frontal poles in two cats and frontal lobes in three monkeys. In the latter animal the posterior limit of the lesion was at least 4 mm. distant from the nearest point from which movement resulted on excitation. Although we obtained striking degeneration of the fronto-thalamic fibres (Dejerine), in these cases the only mesencephalic centre to which we could follow fibres was the upper (*i.e.*, anterior) part of the locus niger. No fibres, therefore, in our experience, go from the non-excitable part of the frontal lobe to the tectum.

A CASE OF ARRESTED DEVELOPMENT OF THE CEREBELLUM AND ITS PEDUNCLES WITH SPINA BIFIDA AND OTHER DEVELOPMENTAL PECULIARITIES IN THE CORD.

BY W. B. WARRINGTON, M.D., M.R.C.P.
Physician to the David Lewis Northern Hospital, Liverpool.

AND

KEITH MONSARRAT, F.R.C.S.EDIN.
Surgeon to the David Lewis Northern Hospital, Liverpool.

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II.—Naked-eye appearances of brain and cord.
III.—Histology of the brain.
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V.—Commentary.
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WE have been induced to place this case on record by the fact of its exhibiting what appears to be an undescribed combination of deformities of the nervous system, all of which seem to us to be of much interest from the developmental standpoint. One of us (W. B. W.) has made himself responsible for the examination of the brain, the other (K. W. M.) for the clinical history and the examination of the cord.

I.—CLINICAL HISTORY.

E. M. H., a female infant, aged six weeks, was brought to the Infirmary for Children, Liverpool, on August 10, 1901. Family history as follows:—A grandmother and aunt died of phthisis; the mother has one other child living; after marriage she had two miscarriages, then the eldest living child was born, then followed another miscarriage and then this child was born.

Anamnesis:—At birth a swelling was noticed at the lower part of the back; from this a creamy fluid was discharged for one day after birth; it grew larger and then gradually smaller after the discharge had recommenced. The mother noticed that the head was enlarging at the third week. The child was born with club feet and without any use in the lower limbs ; she also had *prolapsus ani.*

On August 12 it was noted—there is a linear ulcer with a few granulations over the posterior aspect of the fourth and fifth lumbar vertebræ ; the spine is bifid here but there is no bulging. There is well-marked hydrocephalus. The eyes are prominent ; measurement from external auditory meatus to external auditory meatus is 9⅝ in. ; from root of nose to external occipital protuberance 10⅛ in. The child shows no sign of being able to see but can hear. There is talipes equino-varus of the right foot ; the child moves the hands and arms freely but the legs are completely paralytic.

August 13.—Operation was undertaken to endeavour to drain the cerebro-spinal channels from the lumbar region. A flap was turned upwards exposing the second and third lumbar spines and laminæ, the latter cut and a tightly distended tube of membranes exposed; this was closed below at the level of the fourth lumbar by cicatrix. This tube was opened and a bunch of horse-hair strands passed into the opening; the other ends were carried laterally into a bed dissected up for them between the muscular layers and the peritoneum. The wound was entirely closed.

For the first four days this drainage appeared to act satisfactorily, but on the fifth there was a considerable amount of tension of the structures around the wound, so much so that it was necessary to remove the stitches; a slight amount of cerebrospinal fluid came away into the dressings, but the drainage was much less satisfactory and the hydrocephalus persisted after showing at first some diminution. This condition of affairs continued until August 24, when the child showed signs of gastrointestinal disorder, with vomiting and diarrhœa ; she died on the 29th. The temperature chart shows nothing calling for comment, except for a rise of temperature on the 24th, at the commencement of the attack of gastro-enteritis; there was apyrexia throughout.

II.—NAKED-EYE APPEARANCES OF BRAIN AND CORD.

Post-mortem Examination (August 29).

The cranio-vertebral cavity was opened throughout its extent, In the lumbar region an unhealed wound marks the position of the operative procedure; the arches of L. 4 and L. 5 are represented by stunted projections from the lateral aspect of each body; the arches of L. 3 and L. 2 have been removed. At the level of L. 4 the meninges and contents pass into a dense mass of cicatrix; above this the dura mater appears unusually tough and thick throughout. At the level of D. 4, the whole of the structures in the canal, membranes and contents, are divided into two apparently equal halves, an exostosis proceeding from the centre of the posterior aspect of the body of the vertebra, passing backwards between the divided cord and membranes, and then curving to the right and becoming attached to the right lamina near its junction with the spinous process. To the naked-eye the spinal roots appear normal. Above and below the exostosis the cord and membranes are undivided.

On slitting up the dura mater of the cord, this latter structure is found to be embedded in a casing of loose friable material, from the lumbar region to the cervical, where it becomes gradually less marked. The appearance of the cord after dissection from this bed is seen in the photograph (Plate I). It is a delicate attenuated structure; below there is no cauda equina distinguishable, but the cord becomes involved in the cicatricial mass at the level of the spina bifida.

The upper extremity of the cord is marked off from the medulla oblongata by a V-shaped depression, terminating in the well-marked anterior fissure. There are no prominences corresponding to the anterior pyramid and olive, and the medulla passes insensibly into the pons, no trace of the thickening caused by the transverse fibres of the pons being visible; the median raphé is well-marked, and on each side of this, opposite the rudimentary cerebellum, a slightly elevated ridge is present. The crura-cerebri emerge from beneath the thickened upper extremity of the pons, attached to each other mesially for some distance before dividing to enter the hemispheres. The optic chiasma and tracts are of normal appearance, and the corpora albicantia well formed. On the posterior surface, faint longitudinal lines indicate the fasciculi of the cord at its upper extremity. The inferior peduncle is very poorly represented. The cerebellum is represented by a very rudimentary structure with a few leaflets; it is impossible in this to distinguish the various parts; the worm is represented by a small oval prominence. The superior peduncle consists of a delicate flattened band of tissue on either side. The mesencephalon is represented by a single large structure; no trace of a division into anterior and posterior corpora quadrigemina being seen; the optic thalami are of moderate size, and the soft commissure is well formed.

The cerebrum exhibits marked flattening of the convolutions and extreme dilatation of the lateral and third ventricles. With these exceptions the hemispheres exhibit no peculiarities.

After removal the brain and cord were immersed in Muller's fluid.

III.—HISTOLOGY OF THE CEREBELLUM, MEDULLA, PONS, AND MESENCEPHALON.

The series of figures accompanying this article shows that we had to deal with a case of defective development of the cerebellum and of all those parts of the central nervous system which are connected with that organ. It is on account of the complete nature of this agenesis and the manner in which it is chiefly confined to the cerebellum and its annexes, that the interest of the anatomical findings in these regions arises.

Cerebellum.—The extremely rudimentary character of this organ was found to be accompanied by a similar absence of histological development.

The figures given represent accurately the outlines of its convolutions, which it will be at once seen were of an extremely simple nature. In many places the organ was entirely unconvoluted, and represented by an undifferentiated mass of embryonic tissue and small cells.

It was impossible to recognise the various named lobes. The lateral parts of the organ seemed to be slightly better developed than the remaining part of the hemispheres, and here were found almost the only myelinated fibres present. In these regions also, in a few parts, a differentiation into a cortex with its three layers of granular and molecular strata and Purkinje's cells could be seen.

No trace could be found of central gray nuclei. It is to be especially mentioned that there was no evidence of sclerosis, or of vascular degeneration.

The bulb.—The well-defined column of Burdach could be traced into the corresponding nucleus, the cells of which were large and numerous. It is doubtful whether a nucleus gracilis could be distinguished; this nucleus commences normally at a lower level than the cuneate nucleus, and is situated medially. The first cell mass to appear in tracing the posterior columns upwards was situated laterally, and evidently in connection with the fasciculus cuneatus. The condition of the cord, especially in the lumbar region, is to be regarded as the explanation of this appearance. From this nuceus internal arcuate fibres were seen streaming inwards, fairly numerous and well coloured by the Weigert stain. Their decussation and the upward continuation of the fillet were well seen. The pyramids and their decussation were also fairly well coloured, though not so markedly as the fillet system.

No trace of the inferior olives or of accessory olives was found. Their usual position was represented by a well-defined area of embryonic tissue, entirely devoid of medullated fibres or of cells having any resemblance to the cells of the olives (figs. 5 and 6). External arcuate fibres, both anterior and posterior, were absent. Nuclei arcuati could not be recognised.

The cerebellar peduncles.—The three peduncles of the cerebellum were practically absent. The restiform body begins in normal brains to be visible on the outer side of the superior extremity of the nucleus cuneatus, but this region was almost devoid of medullated fibres. In the pons, where it is situated between the two roots of the eighth nerve, there was found a scanty number of irregularly-arranged myelinated fibres.

Both the corpus restiforme proper and its inner part appear almost unrepresented; no vestibulo-cerebellar fibres can be traced, although, as will be stated later, the end nuclei of the vestibular nerve appear well developed. The absence of the major part of the inferior peduncle is, of course, to be considered as connected with the absence of the olives and the scanty development in the cord of the direct cerebellar tract and posterior columns.

The figures show that the transverse fibres of the pons and middle peduncles were almost entirely absent; a few sections showed a band of medullated tubes situated laterally, which apparently represented all that existed of these structures.

The pyramids were seen to be lying in a mass of embryonic tissue. No trace of pontal nuclei could be discovered.

It would appear also that the superior peduncle was absent, a condition to be expected, considering that the nucleus dentatus and nucleus ruber could not be found.

Perhaps a few fibres in fig. 12 are to be considered as belonging to that system, and in the mesencephalon there is a decussation corresponding chiefly to the fibres of Meynert and Forel, but which may in part represent the superior peduncle.

The nuclei of the cranial nerves and tegmentum.—The deep origins of the cranial nerves were readily seen, and the various cell groups seemed normal.

Especial interest centres in the eighth pair. The large ventral cochlear end nucleus is well formed, and the lateral fillet system normal. The superior olives and corpora trapezoidea are well coloured by the Weigert stain. Fibræ acousticæ are present, but not numerous.

With regard to the end nuclei of the vestibular nerve, so far as the method used will permit of observation, these cell groups were seen to be well represented, both by the central inner nucleus and the outer group of cells composing Deiters' nucleus. The various central and spinal fibres from these end nuclei could not however be recognised; in particular it was certain that no fibres passed into the cerebellum.

The posterior longitudinal bundle was well represented, but in the upper part of the pons, instead of occupying its usual position almost immediately beneath the fourth ventricle, it was seen to be separated from this by a mass of embryonic tissue (see fig. 11).

The nuclei tegmenti were fairly well seen.

Mesencephalon.—We have already mentioned the striking naked-eye appearance of this structure. On section the noticeable features were the entire absence of the red nuclei. The series of sections failed to reveal anything which resembled this important structure. The superior peduncles also were absent, with, perhaps, the exception of the rudimentary decussating fibres already alluded to. The feeble development of the colliculi of corpora quadrigemina also arrested attention. In the pes the slight extent, laterally and medially, of the medullated tract, would appear to indicate that the *pars pyramidalis* only was represented—the fibres connecting the frontal and temporal lobes being absent. The third nucleus, fillet system, substantia nigra and fountain decussations were well seen.

IV.—Histology of the Cord and Membranes.

Cord.—The cord after fixation and hardening in Müller's fluid, was divided into twenty-four portions, each of which was embedded in paraffin. Sections from each were stained (*a*) by the Pal-Weigert method, after impregnation with Marchi's fluid ; (*b*) with hæmatoxylin and other chromatin stains.

The appearances found in sections from eight different levels will be described here, and any important points in intermediate sections also noted.

Series I. Upper Cervical (fig. 14).—The cord is reniform in shape. The central canal is represented by two channels; in section each shows as a slit, one transverse, the other antero-posterior. The transverse channel is lined by columnar epithelium, but only over part of its wall; the antero-posterior portion extends from within a few lines of the centre of the transverse towards the posterior margin of the cord; it is unlined by epithelium but bound by a membrane; between its anterior end and the transverse slit is neuroglial connective tissue. That these two portions each represent part of the canal is shown by the fact that they become continuous at a lower level. There is no trace of a posterior commissure. The gray matter shows numerous nerve-cells in the anterior horns, the medial, the anterior and the antero-lateral groups being well shown, the postero-lateral less so. The white commissure shows numerous medullated fibres. In the white matter medullated fibres are scanty throughout ; there is a well-marked postero-external tract, however, and in the anterior ground substance medullated fibres are also fairly numerous; they are few and scattered in the direct cerebellar, antero-lateral ascending and descending tracts, and in the positions of the pyramidal tracts, and absent entirely in the position of the postero-internal column. In the latter locality and elsewhere, a fine neuroglial substance makes up that part of the cord outside the gray matter. The substantia gelatinosa is a very prominent structure.

Series II. Middle Cervical (fig. 15).—The canal is in the shape of a T, the vertical limb running towards the posterior aspect; the transverse slit is alone lined by columnar epithelium, and that in part only. In the gray matter the grouping of the cells is not distinct except that the mesial column is well marked; the cells of the lateral groups are numerous; the fibres of both anterior and posterior roots are distinctly medullated. Burdach's column is again well marked off, and contains numerous medullated fibres; the anterior ground substance also shows a considerable amount of medullation; but as before these fibres are few in the direct cerebellar, the pyramidal and the antero-lateral ascending and descending tracts, and absent entirely from the position of Goll's column. The medullated fibres in Burdach's column do not extend to the periphery of the cord. The substantia gelatinosa is as before a well-marked structure.

Series III. Lower Cervical. The Cord (fig. 16) is more flattened from before backwards than in the last series. This series is taken from the lowest cervical zone. The outline of the canal is in the form of a long transverse limb, and a short posterior extension from the centre of this. It is lined discontinuously with columnar epithelium; the apical part of the posterior limb is so lined, but not the remainder of this limb. The arrangement of the gray and white matter resembles that in the last series, that is to say, the postero-external column and the anterior ground substance are fairly well occupied, the remainder of the cord outside the gray matter being almost entirely without medullated fibres; in the gray matter the cells are numerous and well formed. By the lateral extension of the canal the anterior and posterior horns are cut off from one another. On the ventral aspect of the canal are a few medullated commissural fibres.

Series IV. Upper dorsal; just above the level of the division (fig. 17).—The cord is here a flattened ribbon-like structure, consisting of two lateral masses connected by a narrow strip. The canal extends from side to side across the middle line; on the one side it has a branched outline, on the other it is much smaller and spherical, the two lateral dilatations being joined by a slit with a narrow lumen; the epithelial lining is partial, the greater part being unlined. The gray matter is well represented on each side; in the anterior horns the mesial and lateral columns are large groups; by counting the cells of several sections it is found that the number is practically the same on each side. The only medullated fibres are a few in what appears to be the position of the postero-external column; the remainder of the cord structure is a fine gliosal tissue with numerous small cells.

Series V. At the level of D. 4; that is to say, at the division (fig. 18).—The halves of the divided cord are of about equal size, and irregularly circular in outline. The canal is represented on each side, but more extensively on one than on the other. On the left side the outline of the channel is oval, and it is completely lined by columnar epithelium; on the right side the outline is branched, and in some sections the branches appear as definite diverticula separated from the central channel by encroaching glial tissue. The cells in the anterior horns of each side are about equally divided in number; they are in two groups, one near the mesial, the other near the lateral margins of the horn. The amount of tissue outside the gray matter is now very scanty and staining with Pal-Weigert does not exhibit the presence of any medullation. The vascular spaces throughout the cord are large and numerous; that is to say, there appears to be unusual vascularity here.

Series VI. Lower dorsal; below the division (fig. 19).—The two halves have now reunited and form a cord of very diminished dimensions and reniform in shape. Here a remarkable change is met with, in that the central parts are disintegrated into a tissue of coarse fibrillar structure in which are numerous irregular cavities. This disintegration has taken place posteriorly to the central canal, which is a transversely elongated slit. The outline of the canal is, however, largely obscured and the lumen invaded by the process of disorganisation. In addition to the coarse fibrillation of this disintegrated area, there are a large number of "colloid bodies" present throughout it, and also a few giant cells; fragments of columnar epithelium, evidently derived from the lining of the invaded central canal, are also found here and there; there is no round cell infiltration or any evidence that the process of change is of an inflammatory origin. There are a few well-formed ganglion cells in the anterior horn on each side. No trace of medullation in the fine gliosal tissue which constitutes the circumferential part of the cord.

Series VII. Mid-lumbar (figs. 20 and 21).—The cord is here reduced to very small dimensions; the kidney shape is noticeable. There are traces of the disintegrating process noted in the series above, but it is much less marked here; the sections show that this disorganisation, commencing at about D. 6 or D 7, reaches its maximum in the lower dorsal region, and disappears in the lumbar portion of the cord above the level of the spina bifida.

In this series there is no marked differentiation between gray matter and white matter; the whole structure is a fine gliosal tissue, the only exception being the presence of a few ganglion nerve-cells in the position of the anterior horns on each side. The outline of the central canal is slit-like from side to side, lined only in part by columnar epithelium.

Series VIII. Level of the spina bifida.—At this level the nervous tissue is represented by a central structure representing the cord, by nerves, nerve-roots and ganglia. All are embedded in a fine connective tissue containing numerous large vascular channels. The cord is more flattened than in the last series but is kidney shaped; there are a few nerve-cells in the position of the anterior horn on each side; no medullated fibres. The posterior ganglia exhibit numerous well-developed ganglion cells, but also show a marked hypertrophy of intercellular substance consisting of a highly cellular connective tissue.

Membranes.

Histologically the dura mater is of well-developed fibrous tissue. Within this the distinction of other coverings is entirely obscured by the material in which, as already described, the cord is embedded. This material consists of a highly cellular connective tissue containing numerous large thick-walled blood-vessels.

Ganglion Cells of the Cord.

Cervical region.—In this region there are three well-defined groups in the anterior horn. (*a*) Mesial column—large cells ten to fifteen in number. (*b*) Ventro-lateral column ten to twelve in number. (*c*) Dorso-lateral column, the largest of the three groups, seventeen to twenty cells. The numbers indicate the cells counted in each section and averaged.

Centrally to the dorso-lateral group are scattered cells of small size not marked off into groups but most numerous in the position of the middle cell column. No defined Clarke's column. No cells in posterior horn.

Upper dorsal region.—The cord here is elongated laterally. There are two well-defined groups of cells in the anterior horn. (*a*) Mesial group, large cells six to eight. (*b*) Lateral group not (subdivided) cells twenty-five to thirty in number. Between these groups but more centrally placed are a few scattered cells of small size five to seven in number. No cells in posterior horn.

Mid-dorsal region.—The total number of cells is smaller. The mesial and lateral groups are well defined and contain about an equal number of cells, twelve to eighteen in number, in different sections. There are also a few centrally situated, five to six in number. The cord is here divided. Immediately below the division—the mesial group is large—of large cells, fifteen to sixteen in number; the lateral group is composed of smaller cells, four to eight in number.

No cells outside these *two* groups.

Lower dorsal region.—The ganglion cells are, with the exception of a few scattered laterally, grouped into one mesial column, eight to ten in number.

Upper lumbar.—Cells very few in number; in some sections none are seen. The average is three in each anterior horn, placed antero-mesially.

Mid-lumbar.—The cells are here more numerous than in the upper lumbar region; they are in two groups, counted in eight sections at different levels:—

(1) Antero-mesial, 4, 3, 4, 2, 6, 1, 2, 4.

(2) Antero-lateral, 3, 1, 4, 3, 3, 5, 3, 2.

Sections of the posterior root ganglia show the cells to be numerous, large and well formed.

SUMMARY.

A child aged six weeks, presenting a lumbar spina bifida ruptured at or before birth, and now healed; hydrocephalus; paraplegia of the lower limbs. Death from intercurrent gastro-enteritis.

(1) In the brain. Arrested development of the cerebellum and of its efferent and afferent fibres, and of their nuclei of origin; of the restiform bodies, the olives, accessory olives, external arcuate fibres and nuclei arcuati; middle peduncles and transverse fibres of the pons, pontal nuclei, vestibulo-cerebellar tracts; superior peduncles, gray nuclei of cerebellum, red nuclei of the tegmentum; possibly the cerebro-pontal cortical tracts.

(2) In the cord. General attenuation of this structure throughout, division at the level of the fourth dorsal vertebra into two equal halves; marked enlargement of the central canal which divides with the division of the cord; the presence of various irregular cavities in the cord and disintegration of its central parts in the lower dorsal region; normal development of the gray matter with well-formed ganglion cells; scanty development of white matter, its place being taken by tissue of neuroglial structure.

(3) The coverings of the cord. The whole cord, as far as the upper cervical area, embedded in a fine connective tissue with large vascular channels; the laminæ and spines of the fourth and fifth lumbar vertebræ deficient; an exostosis dividing the canal at the level of the fourth dorsal vertebra.

V.—Commentary.

The case exhibits a condition which may be generally described as arrested development of the central nervous system from the mesencephalon downwards, with a superadded local process of degeneration. In addition to this the abnormalities in the parts contiguous to the cord are to be considered, and on these we may first comment.

I.—The deficiency in the completion of the bony casing affects that section where the deformity is most commonly present. The exostosis which divides the canal and its contents is a rare developmental fault, but there are records of several cases presenting similar bony septa. Thus in the report of the Clinical Society on spina bifida four examples of this variation are recorded (1). One at the tenth dorsal vertebra, the whole of the laminæ and spines below being deficient; one in the lower dorsal region at the apex of a spina bifida involving the whole canal below, associated with an entirely bifid cord below; a third exhibiting a similar condition in the lumbar region, but with union of the cord below the exostosis; the fourth concerns a spina bifida of the last two dorsal and the upper two sacral vertebræ, the cord being divided into unequal parts and reuniting below.

M. Houël (2) has described a case in which a similar exostosis projected from the bodies of the third and fourth lumbar vertebræ, with its apex partially occluding the opening into the sac of a lumbo-sacral spina bifida; the cord at the point being divided into two parts and reuniting below. Sulzer (3) found in a lumbar spina bifida complete division with reunion below of the cord, apparently due to a similar exostosis.

It will be seen that these cases present one marked point of difference from that described here in that the exostosis and the division of the cord was in immediate relation with the deficiency in the vertebral arches constituting the spina bifida. M. Houël was of opinion that the exostosis in his case was in direct casual relationship with the deficient laminar junction; on general grounds and in the light of this case it appears more reasonable to consider this variation in cases of spina bifida as merely concomitant, the deficiency in the laminæ and spines and the growth of such exostoses being all faults in the development of those groups of cells which form normally the bony casing of the cord. Another feature in which this case appears to differ from others similar is in the division of the meninges into two entirely separate tubes, each encasing one half of the cord. Apart from the presence of an exostosis such as was found in this case, the association of division of the cord and spina bifida has been recorded by several, *e.g.*, Recklinghausen (4), Koch (5), Ollivier (6). A division of the cord, a rachischisis, also occurs unassociated with spina bifida. A case of this kind is related by Recklinghausen (7), and another has been recorded by Foá (8). In each case, as in our own, the division was into two approximately symmetrical halves, with gray matter and white matter normally distributed, and with a central canal in each half. One of us (K. W. M.) has recently had the opportunity of dissecting a specimen which is also of interest in connection with this rachischisis. A fœtus born at full term exhibited a condition of anencephaly with spina bifida involving the cervical and dorsal regions. The nervous tissue representing the spinal cord was in the form of a tube with membranous wall, on opening which four prominent longitudinal ridges were seen to bulge into the lumen, arranged symmetrically, two on each side. These were found to consist of myelinated nerve-fibres; at the lower dorsal region the separation into two halves became distinct; on the right side the two ridges united to form a rounded cord, on the left the nervous tissue remained diffusely distributed on the inner surface of the membranous covering. The separation into right and left halves was complete but unsymmetrical.

This case and those of Recklinghausen and Foà, show that apart from the presence of a mechanical obstruction, a rachischisis occurs as a developmental fault, *sui generis;* in place of the union of the dorsal and ventral columns of nervous tissue on each side through the medium of the roof and floor plates to enclose a single canal, each dorsal column unites with each ventral column and the floor and roof plates default. In the process of union of the dorsal with the ventral column, a portion of the lateral extension of the central canal is cut off, and in this way a channel is present in each half.

The presence of an exostosis, as in this case here recorded, affords an easy explanation of the etiology of the rachischisis; in the absence of such a condition the explanation of the division is not forthcoming; it is one of the rarest of deformities.

The tissue in which the cord was embedded is of much interest. At first sight it seemed probable that it was of the nature of an inflammatory effusion, but the histology entirely negatives this. The structure indicates an origin in mesoblast, in that portion of mesoblast which extends backwards in a double fold to enclose the neural tube, and which is spoken of by embryologists as the membranous primordial vertebral column, and from which the cutis, the vertebral arches and the cord coverings originate. As an erroneous developmental product it belongs to the same category as the maldevelopment of the vertebral arches. We are not aware of any quite similar observation recorded; Recklinghausen (9) has, however, placed on record a case of spina bifida occulta, in which a myofibrolipomatous tissue occupied the spinal canal in the lumbar region, and encircled the cord[1]; the structure in our own case is also analogous to that described by Mr. Bland Sutton (10) in the variety of spina bifida to which he gave the name myelocele. In this variety the medullary folds coalesce imperfectly, the central canal opens dorsally, and the tissue surrounding the furrow which is its continuation, shows microscopically nerve-cells, neuroglia and a few nerve-fibres embedded in a nævoid mass of dilated capillaries and connective tissue.

II.—Probably in the great majority of cases of spina bifida there exists also some developmental peculiarity in the cord. Even in cases of the uncommon simple meningocele, the cord not unusually shows some abnormality; *e.g.*, in a case of apparently simple meningocele lately examined by one of us (K. W. M.), the cord exhibited a marked degree of hydromyelia above the level of the spina bifida.

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[1] *Cf.* also Gowers' *Trans. Path. Soc.*, xxvii., 19.

The case now under consideration shows this involvement of the cord in an extreme degree. The central canal is not only of very large dimensions throughout, but its outline is similar, generally speaking, to that which is found in the embryo up to about the eighth week, at any rate in the cervical region of this case. The way in which the posterior limb of the canal is closed by the approximation of its lateral walls gives strong support to the belief that the posterior median septum (the so-called fissure) is normally formed by the growing together walls of the dorsal part of the canal. It is not easy to explain the deficiency of the lining of cylindrical epithelium over a considerable proportion of the wall of the canal; it appears necessary to attribute it to the increased area of the wall and the consequent proportionate deficiency of those cells which normally are sufficient to give the canal a complete lining. A similar deficiency has been noted by Chiari in cases of hydromyelia recorded by him (11). The ependyma is, however, a formed structure very early; the cells are ciliated in the human fœtus at the fifth week, and line the large canal, but this is, of course, of a much smaller surface area than the canal in the cord we are describing.

In the tissue of the cord itself the condition of first importance is that its substance is to a very large extent of a fine neuroglia structure, with marked defect in the development of the nervous elements proper. It must be remembered that the neuroglia is of epithelial origin, and derived from the cells of the neural tube; it is therefore the less specialised of the two elements which arise from these cells, and the development of the more specialised is at fault in this case. It is well known from the pathological anatomy of syringomyelia how frequently associated are abnormalities of the central canal and the presence of undeveloped embryonal nervous tissue of a fine neuroglial structure. The presence of this glia tissue is differently explained; on the one hand it is widely held that in most cases the syringomyelia is secondary to an actual hyperplasia of glia tissue, a gliomatosis, an over-production; on the other hand a second view holds that the original starting point of the cavity formation is the presence of undeveloped glia tissue which should have been transformed, but which persists owing to the want of the normal guidance to transformation

It seems clear that the preponderance of glia tissue in our own case is to be ascribed to checked development and arrested specialisation. v. Leyden (12), who holds that this glia tissue is a manifestation of developmental defect, recorded some years ago two cases of much interest for comparison with our own: one a child, aged two years, with syringomyelia enclosed by layers of embryonal glia tissue, and associated with encephalocele and a rudimentary cerebellum; the second case, a child aged two and a half years, with hydrocephalus, rudimentary cerebellum, and syringomyelia, accompanied by undeveloped embryonal glia tissue. Apart, however, from the distended central canal, we have in the lower dorsal region a localised area in which this embryonal tissue has undergone a definite degenerative process with resulting excavation of the central parts of the cord. Of the exact causation of this excavation we are unable to express a confident opinion. As before stated, there is no evidence which enables us to state that it occurred as a result of any actual inflammatory process strictly so called. The two most striking points in the histology are the presence of the "colloid bodies," and the occasional occurrence of a giant-cell system. The origin of these colloid bodies, which have been described in a variety of degenerative processes in the central nervous system, is variously interpreted. They are supposed by some to arise from myelin set free by the degeneration of the myelinated fibres, but this origin is out of the question here as there is no myelination in the region where they are found. The giant cell is, in our opinion, always a degeneration product, as a rule associated with the destruction wrought by a chronic inflammatory process, such as tuberculosis and syphilis. On the whole we consider that the evidence is in favour of the incidence of an active disintegrating influence supervening on the congenital abnormality, and not of a simple degeneration from inherent or autonomous causes.

The case exhibits in a striking way the association of hydromyelus, gliosis, and true syringomyelia. It is known from the researches of His (13), Lenhossek (14), and others that the ependyma and neuroglia possess a common developmental origin; it is not surprising, therefore, to find abnormalities of the one associated with abnormalities of the other. Hoffman and Schlesinger have stated the dependence of the central gliosis, which is the basis of the majority of cases of syringomyelia, on a primary hydromyelia of the central canal; however this may be, the association is easily understood. As we have seen, in this case the central cells have provided but a partial lining for the canal, the remainder being lined by tissue of glia structure similar to that which constitutes the remainder of the cord outside 'In relation to the genesis of syringomyelia the view is commonly held that a true hyperplasia of glial tissue is the first product, but authorities differ as to the question of referring this "gliosis" to a congenital abnormality. Hoffman says (15) "the basis and origin of the disease process is in most cases a congenital developmental anomaly, whereby nests of embryonal tissue remain behind the normal central canal; a plicated central canal possesses the same importance." Similarly Schlesinger: "I consider that the central gliosis originates in the central canal epithelium; with this are found for the most part other congenital anomalies, especially widening of the central canal; that the excavation of the new-formed tissue results from degeneration of the same, dependent on vascular abnormalities."

The case here before us does not conform to the most commonly observed type of syringomyelia in that there is no evidence of anything that can strictly be called gliosis or local proliferation of glia cells; but the whole cord shows a condition of gliosis, if this term means the presence of young glia tissue, and it is in this posterior to the central canal that the degeneration and excavation is taking place. *It shows this cavity formation in progress, and its connection with an undoubtedly developmental anomaly.*

In Series IV. it is seen that on one side the canal has a branched outline, and that the branches tend to be cut off from one another by the encroachment of their walls; in this way also cavities partially or entirely lined by epithelium arise. It is doubtful whether persistent cavities in the cord result from such a process as this, as it appears probable that they will in the process of growth be encroached on to their obliteration.

The absence of myelinated fibres throughout the greater part of the cord is a matter which calls for remark. It is known that in cases of spina bifida where the cord is embedded in the sac wall, both it and the nerves originating from it exhibit an entire absence of medullated fibres. An example of this peculiarity is reported by the Clinical Society's Committee.

In our own case the number of myelinated fibres is very scanty throughout the whole cord, and they are chiefly absent from the system tracts throughout. These fibres are present only in (*a*) the anterior and posterior roots, and (*b*) the postero-external column, and the ground fibres of the antero-lateral region, that is to say in the ground tracts above the division of the cord. It is in these regions that the fibres normally first acquire their medullary sheaths, and the arrested development of this case confirms in this way the information which has been derived from the study of the natural process.

III.—A considerable number of cases of atrophy of cerebellum have been recorded since Combette's often quoted paper in 1831. Many of the earlier cases were not examined microscopically, or only by the older, obsolete methods, and hence do not possess much anatomical interest. In the last ten years however, several detailed and valuable accounts of this condition have appeared, notably the papers by Menzel, Max Arndt, Spiller, Thomas and Dejerine (*vide* Appendix). These writers also give a fairly complete account of the literature, especially is this so in the detailed analyses given by Thomas in his "Thesis on Le Curvelet." Ferrier also in "Allbutt's System" tabulates the cases since 1879, correlating the clinical symptoms with the anatomical findings. He thus completed the list given by Nothnagel in his "Tophische Diagnostik."

Lastly, quite recently Dejerine and Thomas have given an account of a case with an unusual pathogenesis. The origin of these conditions, indeed, varies very greatly, and in an appendix we have endeavoured to classify the cases on a basis on what appears to be their mode of origin. The clinical interest of many of the cases is considerable, first because they show the symptoms resulting from simple defect of this organ, and secondly, because of the increased interest which these observations have thrown on the nature of the hereditary ataxia of Marie, Friedreich's disease, and certain allied conditions. The clinical aspect of the subject does not now concern us, but we may mention one fact which appears to be very clearly illustrated by a study of the cases, viz., the same symptom group may appear with very different anatomical lesions. Thus, the cases of Nonne and Muira showed a simple smallness of the cerebellum. Spiller's is one of sclerotic atrophy, Menzel's of sclerotic atrophy with lesions of the cord, and Meyer found that the cord alone was affected, yet in all these cases the symptoms were closely allied.

The interest in the present case is for the most part anatomical; in the brain at least the condition appears to be one simply of arrested development, and owing to its completeness the relationship which exists between the cerebellum and its annexes is demonstrated in its main features with remarkable clearness, and confirms if it does not add anything new to our knowledge on this subject.

As to the date at which the development became defective it is difficult to say; it must have been very early, for the olives can normally be made out at the end of the third month. The growth of the organ must, however, have been irregular, for Purkinje's cells, which were found to some extent, usually only appear about the sixth month, whilst the corpus dentatum, which also, according to Obersteiner, appears at that time, was absent.

The majority of anatomical findings which we hope will be obvious from a consideration of the figures and the text, do not require any comment, they contain what is established both by a study of similar cases and by various other methods of research.

A few points merely may be mentioned.

The absence of external arcuate fibres, combined with the integrity in part at least of the dorsal column nuclei, has been noticed by a good many observers, as in the cases of Menzel, Arndt, Cramer, Thomas, and Spiller. In these cases the nuclei arcuate were also absent, and the fact suggests, as Bechterew supposes, that these cells form relay nuclei. Menzel believes some of these fibres arise in the cerebellum.

So far as the method employed permitted, no atrophy was noted in the nuclei reticularis tegmenti; the cells appeared numerous and large. This is important in view of the finding of Cramer in his case of unilateral atrophy, that the nucleus on the contra-lateral side was atrophied. Cramer contends that his case shows the connection of this nucleus with the middle peduncle.

The fasciculus centralis tegmenti is described by Bechterew and Flechsig (*Neurolog. Centralb.*, 1885) as a descending tract terminating in the olive and forming by this body a connection between the lenticular nucleus and cerebellum. It is situated just external to the inferior olive, and higher up between the superior olive and fillet. Spiller believes it was atrophied in his case, and in ours also it cannot be seen. Short tegmental fibres appear numerous and well stained. It is also of interest to note that the fillet and posterior longitudinal bundle were both well developed, notwithstanding the absence of the olive and cerebellum. This is in accord with the experimental results of Ferrier and Turner.

Lastly, we have mentioned that there is some reason to regard the fronto- and occipito-temporal frontal tracts as being undeveloped. This is difficult of explanation, as it is generally regarded that both are corticofugal systems. It may be mentioned, however, that Obersteiner, in the last edition of his "Anatomy of the Nervous System," states that the latter tract is in part corticopetal.

In conclusion, we wish to direct attention to the history of the pregnancies of the mother of this child—two miscarriages after marriage, then a living child, then another miscarriage, followed by the child here described. Such a history suggests syphilis, but no further evidence could be obtained in support of this suggestion. If syphilis was concerned in this case, and we believe that the history of many cases of spina bifida is tainted by this disease, its activity produced a series of remarkable defects in the fœtus.

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(4) *Virch. Archiv.*, Bd. 105, p. 418.
(5) *Beitr. z. Lehre v. d. Spina Bifida*, 1881.
(6) *Traite d. Malad. d. l. Mœlle epiv.*
(7) *Loc. cit.*, p. 409.
(8) *Riv. sperim d. Freniatria*, 1878.
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(13) *Arch. f. Anat. u. Phys.*, 1890.
(14) *Der feinere Band. Nervensystems*, Auf ii., p. 176.
(15) *Deut. Zeitschr. f. Nervenheilk.*, Bd. iii., p. 82.
(16) *Die Syringomyelie*, 1895, p. 188.

APPENDIX.

A Classification of Cerebellar Atrophies arranged on the Basis of their Probable Pathogenesis.

I.—Cerebellum almost completely absent on one or both sides. Condition primarily due to arrest of development.

1. COMBETTE.—*Bull. de la Soc. Anat.*, 1831.

An epileptic idiot died, aged 11. A gelatinous membrane which represented the cerebellum was connected with the medulla by two membranous peduncles. Pons absent. Cord and brain normal.

2. D'ANDRAL.—*Clinique Médicale*, vol. v. (abstract from Thomas, *Le Cervelet*).

A woman died, aged 45. Mentally feeble and liable to incoordinated movements in the limbs. Left cerebellar hemisphere practically absent.

3. LALLEMENT.—*Soc. Anatomique*, 1862.

Patient died from apoplexy, aged 53. No symptoms during life. The left cerebellar hemisphere was absent with the same sided superior peduncle and contra-lateral olive and nucleus ruber tegmenti.

4. LEYDEN.—*Virchow's Archiv.*, lxviii., 1876.

Two infants with meningocele, syringomyelia and absence of cerebellum.

5. HITZIG.—*Archiv. f. Psychiatrie*, xv., p. 267, 1884.

Patient died, aged 38. As a child was of slow intellect, gradually developed symptoms resembling general paralysis, with ataxia of both extremities and oscillation of the body.

Right cerebellar hemisphere reduced to a minimum, middle peduncle and pons with contra-lateral olive absent.

6. FERRIER.—"Functions of the Brain," 1886.

Girl died, aged 15. Mentally feeble, with general muscular weakness and tremors of the hands.

The cerebellum was represented by a minute nodule. Pons and peduncles were absent.

7. NEUBURGER AND EDINGER.—*Berlin Klin. Wochen.*, 1898.

Man died, aged 46. He presented no nervous symptoms but suffered from bradycardia, death from cardiac failure.

Right cerebellar hemisphere practically absent.

Diminution of right superior and middle peduncles with the contra-lateral olive and red nucleus. Diminution in the central gray cerebellar masses and in the left nuclei pontis.

8. This case 1902.

II.—Cerebellum congenitally small, but of normal histological structure.

1. OTTO.—*Archiv. f. Psych.*, p. 730, 1874.

Man died, aged 39. Mentally feeble, but no physical inability.

Cerebellum was very small, pons rather narrow, but brain and cord normal in size.

2. VERDELLI.—*Rivista Clinica*, 1874 (abstracted from Thomas).

Man died, aged 19. Markedly rachitic. Epileptic convulsions from two years old.

Proportional reduction in size of cerebellum, medulla, and pons.

3. NONNE.—*Arch. f. Psych.*, 1891.

Patient died, aged 40. This is one of the cases in which Marie founded his "Hereditary Cerebellar Ataxia." The whole central nervous system was small, but especially the cerebellum.

4. Miura.—*Mittheil. der med. Fac. der Kaiserlich*, Japan univ. *La Tokio*, Bd. iv., Heft 1, 1898. "Abstract from Dejerine and Thomas" (*loc. cit.*).

One of two brothers exhibited symptoms similar to those in Nonne's case. Smallness of the whole central nervous system, especially of the cerebellum.

5. Fraser.—*Glasgow Med. Journal*, 1880.

Another case with symptoms resembling those associated together by Marie. Pathologically the examination was incomplete, but smallness of the cerebellum was the chief lesion with slight histological defects in its structure.

III.—Comprises the majority of cases. There is an atrophy with a general sclerotic condition. The cortex appears primarily affected, either the whole or in part. The disappearance of the white matter corresponds to the extent of cortical defect. There are often indications of chronic meningitis and vascular degeneration. The symptoms are often those of epilepsy with mental enfeeblement, and in a number of cases date from the occurrence of some acute infectious disease in early childhood. It is difficult to discern the exact pathogenesis of these conditions, probably an acute disease acts as an exciting agent in developing a previously existing morbid condition, and leading to retrograde changes in nervous tissue.

The vascular changes are in this division of cases usually secondary in great part.

1. Duguet.—*Soc. Anatomique*, 1862 (abstracted from Thomas).

(α) Woman died, aged 39. No symptoms till 26, then epileptic fits and general weakness developed.

(β) Man, aged 72. No symptoms till three months before death, then convulsions occurred, followed by incoordination movements.

(γ) Patient died, aged 17. Epilepsy since 18 months old.

2. Maynert.—*Wien. Med. Jahr.*, 1864.

Died aged 62, from mitral disease. Symptoms began three years before death. They were incoordination, trembling, and affection of speech.

3. Clapton.—*Trans. Path. Soc.*, London, 1871.

Died at 33 from pleurisy. Measles at 4 years old, and then gradually unsteadiness in walking, enfeeblement of intellect, and inability to properly use his hands.

4 Pierret.—*Archiv. de Phys.*, 1872.

Died aged 69. At 4 had a "fit," and never quite recovered. Staggering gait developed.

Cerebellum, middle peduncle and olives markedly atrophied.

5. **Meschève.**—*Virchow's Archiv.*, p. 559, 1880.

Died aged 40. Epilepsy with mental alteration, rotation in direction of an entering corkscrew. Gait oscillating, speech scanning.

Sclerosis of right cerebellar hemisphere and nucleus dentatus.

6. **Claus.**—*Arch. f. Psych.*, vol. xii., p. 669, 1882.

An insane epileptic.

Partial sclerosis of cerebrum and cerebellum.

7. **Kirchoff** (Case II.).—*Arch. f. Psych.*, Bd. xii., 1882.

Woman of 20 died from phthisis. There was trembling and slow choreiform movements.

Cerebellum was very small and hard. K. believes a sclerotic process had become engrafted to an arrest of development occurring at the seventh month.

8. **Borrell.**—*Neur. Centralb.*, 1883.

Died aged 38. Convulsions and mental defect since infancy, tottering gait, tonic spasm of the muscles of the neck. Pia mater thickened.

Left cerebral hemisphere practically absent, right much diminished. Olives invisible and pons very small.

9. **Mayor.**—*Journal of Mental Science*, 1883.

Died aged 32. Epilepsy and idiocy since birth. No disorder of movement.

Right cerebellar hemisphere sclerosed, with some healthy patches in places.

10. **Sommer.**—*Neur. Centralb.*, 1884.

Died aged 30. Severe cerebral illness at 3 years old; in the latter period of life was subject to psychical agitation, and a peculiar gait of propulsion and staggering.

11. **Ingels.**—*Bull. de la Soc. de Med. de Belgique*, 1884.

A dangerous epileptic. No motor disorder.

Pons as well as cerebellum atrophied.

12. **Boursont**—*Annal. Medico-Psych.*, 1891 (quoted by Thomas).

Four cases of insane persons with atrophy of cerebellum.

13. **Menzel**, 1891.—*Archiv. f. Psych.*, 1891.

Illness began at 34. Ataxia of all limbs, increased knee-jerks. Tetanic-like contraction of muscles of neck. Affection of speech.

Cerebellum very small, absent in parts altogether. Both cortex and white matter markedly affected. Atrophy of pons and pontal nuclei, olives, part of restiform body. In the cord the posterior columns, pyramids, and dorsal cerebellar tract were found diminished in size. Menzel regards the case as one of primary development error, and the spinal lesion as due to a chronic meningitis No evidence of vascular disease or of increased connective tissue formation.

14. Hammarberg.—*Neur. Centralb.*, 1892.

Died aged 24. At 7 years old severe "cerebral inflammation," gradually followed by oscillatory movements and staggering gait.

Both hemispheres the seat of a sclerosis especially attacking the cortex, also patches of sclerosis in the frontal lobe and in left olive.

15. Cramer.—*Beiträge z. Path. Anat.*, Bd. xi., p. 39, 1892.

Died aged 48. Epileptic since 14, with mental alienation. No particular motor disorders.

Left cerebellar hemisphere sclerosed and atrophied.

16. Royet and Collet, 1893.—*Archiv. de Neurologie*, 1893.

Death at 56. Appears to have been well up to age of 48, then developed staggering gait, increased knee-jerks, slight tremors and nystagmus.

Cerebellum hard and sclerosed, with atrophy of the middle peduncle and pons. No microscopic examination.

17. Moeli.—*Neur. Centralb.*, p. 553, 1889.

18. Bond.—*Journal of Mental Science*, p. 409, 1895.

Died aged 60. Mental deficiency since 17.

Ataxia and general tremor. Symmetrical atrophy and sclerosis of all parts of cerebellum.

19. Spiller.—*Brain*, 1896.

At 5 years of age scarlet fever and diphtheria, and since then trouble in walking, gait staggering, mental deficiency. Died at 19 from tuberculosis. A sister affected in the same manner.

Post mortem.—Deficiency of corpus callosum, small size of cerebellum, atrophy of left cerebral hemisphere. Sclerosed areas in the cerebellum with thickened vessels. Atrophy of inferior olives, middle peduncle of pons, and pontal nuclei. External arcuate fibres and nuclei arcuati and diminution of nuclei reticularis tegmenti.

IV.—Primary vascular disease, attended by chronic interstitial inflammatory changes, chiefly affecting the white matter. Comparable to cirrhosis of the kidney.

1. Schutze, 1887.—*Virchow's Archiv.*, 1887.

Death at 43. Diabetes insipidus since infancy. Developed a staggering gait, slow speech, traces of the intentional tremor, gradual paralysis.

Endareritis obliterans of basilar and vertebral arteries. Cerebellum greatly atrophied from a patchy sclerosis, molecular and granular layers little affected, Purkinje's cells showed marked changes. Increase in neuroglia tissue and diseased vessels. White matter greatly destroyed. Dentate nucleus and superior peduncle, olives and middle peduncle were markedly atrophied. Cord normal.

2 **Max Arndt**, 1894.—*Archiv. de Psychiatrie,* 1894.

Death at 70. Symptoms for the last four years. Gait unsteady, ataxic movements with paresis in arms and legs.

Thickening and disease of arteries at base of brain, cerebellar sclerosis, evidence of chronic inflammatory changes in its substance, dilated capillaries, round-cell infiltration, thickened fibrous tissue. In the cortex Purkinje's cells mostly affected, the molecular and granular layers practically normal. The white matter markedly sclerosed, atrophy of middle peduncle and transverse fibres of pons, of olives. Integrity of the nuclei of posterior columns of cord, but some atrophy of fibræ arcuatæ, internæ and externæ.

V.—A primary atrophy affecting the cerebellar cortex, the nuclei of the pons and the inferior olives, accompanied by marked atrophy of the middle peduncle and partial atrophy of the restiform body. No increase of connective tissue or of altered vessels. This atrophy of cells is considered to be comparable to the Duchenne-Aran atrophy of the cells in the ventral cornua.

1. **Thomas**, obs. iv.—*Le Cervelet*, Paris, 1897.

Patient died, aged 62. Symptoms began at 55. Staggering gait, oscillation of the body, scanning speech.

Cerebellar cortex greatly diminished in all its component parts. Gray nuclei intact. In the cerebellar medulla there was distinct diminution of myelinated fibræ. Atrophy of transverse fibres of pons. Middle peduncle, outer part of corpora restiforma, inferior olives, nuclei arciformi and superior external arcuate fibres.

2. **Thomas**, obs. v.

Age 44 at death. Illness began at 25, with progressive enfeeblement of lower limbs, later, mental incapacity, paresis, tremors, universal loss of sensation of all form.

Cerebellar cortex markedly atrophied while white matter only slightly affected. Atrophy of olives, middle peduncle, tranverse fibres of pons, restiform bodies (partially), cells of nuclei of Goll and Burdach, internal and external arcuate fibres. In the cord the posterior and dorsal and ventral cerebellar tracts affected.

3. **Dejerine and Thomas** (two cases).—*Nouvelle Iconog de la Salpet.*, 1900.

Case (1).—Death aged 55. Illness began about 3 years earlier, gradual inability to walk owing to trembling and staggering, speech become scanning in character. No loss of power or of muscle sense, knee-jerks increased.

Atrophy of cerebellar cortex with degeneration and disappearance of afferent and efferent fibres, of olives, and pontal nuclei, while the central gray nuclei were intact with the superior peduncle and nucleus ruber tegmenti.

Case (2).—Clinical history only given.

DESCRIPTION OF FIGURES.

FIGS. 1 to 13.—*A series of transverse sections from the upper cervical region to the superior extremity of the mesencephalon. Drawn by means of Edinger's drawing apparatus.*

FIGS. 1 and 2. Show commencement of pyramidal decussation. Note the scanty peripheral fibres and the entire absence of fibres in the internal dorsal region of the cord. In fig. 2 the nucleus cuneatus is just becoming visible.

FIG. 3. Pyramid has almost crossed.

FIG. 4. Section at level of fillet decussation.

FIG. 5. Level of usual site of inferior olive, here represented by embryonic tissue. Note scanty peripheral fibres representing the spinal cerebellar tracts.

FIG. 6. Upper level of inferior olive, commencement of vestibular root and rudimentary corpus restiforme.

FIG. 7. Commencement of lateral fillet system, the anterior region of pons entirely devoid of nerve-fibres.

FIG. 8. Level of sixth and seventh nerves.

FIG. 9. Section of maximum development of the cerebellum.

FIG. 10. Level of fifth nerve. Note absence of transverse fibres in pons, possibly the medullated tract situated laterally is a representative of these.

FIG. 11. Upper level of pons.

FIG. 12. Lower part of mesencephalon. Note limited area occupied by medullated fibres in the pes. Well-marked fibres of Meynert and Forel, and perhaps also some representative of the superior cerebellar peduncle.

FIG. 13. Level of third nucleus. No nucleus ruber tegmenti seen.

FIGS. 14 to 21. A series of transverse sections from the upper cervical region to the upper lumbar, described in the text.

ABBREVIATIONS.

pyr. = pyramid.
s.g. = substantia gelatinosa.
n.c. = nucleus cuneatus.
dec. fil. = decussation of the fillet.
des. rt. v. = descending root of fifth cranial nerve.
cor. rest. = corpus restiforme.
cor. trap. = corpus trapezoideum.
s. ol. = sup. olive.
n. coch. = Cochlear nucleus.
n.d. = Deiters' nucleus.
n.c.v. = nucleus centralis vestibularis.
p.l.b. = posterior longitudinal bundle.
n. v. = fifth nucleus.
s. ng. = substantia nigra.
dec. M. & F. = decussation of Meynert and Forel.
a.r.f. = anterior root fibres.
ant. horn = anterior horn.
g.c. = Goll's column.
post. r. = posterior root.
c.c. = central canal.
a.g.s. = anterior ground substance.
a.f. = anterior fissure.
ar. deg. = area of degeneration.

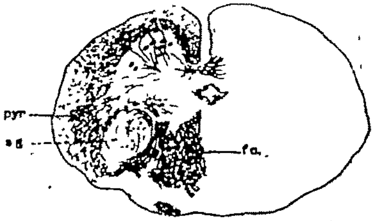


FIG. 1.

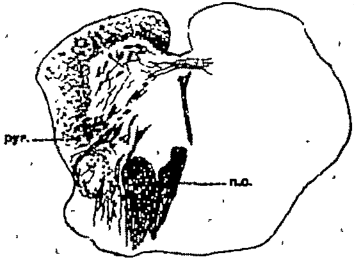


FIG. 2.

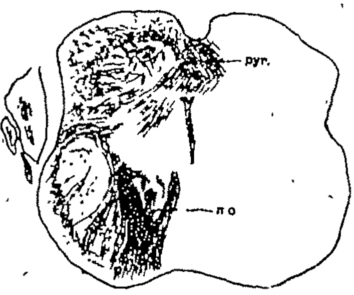


FIG. 3.

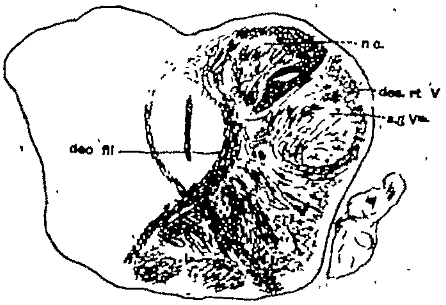


FIG. 4.

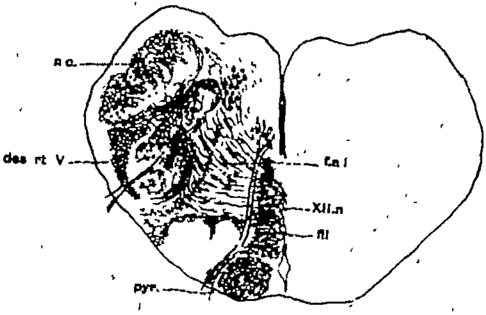


FIG. 5.

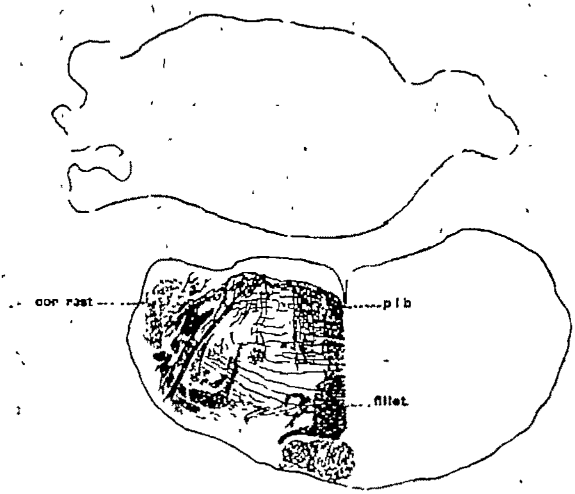

cor rest
p l b
fillet

FIG. 6.

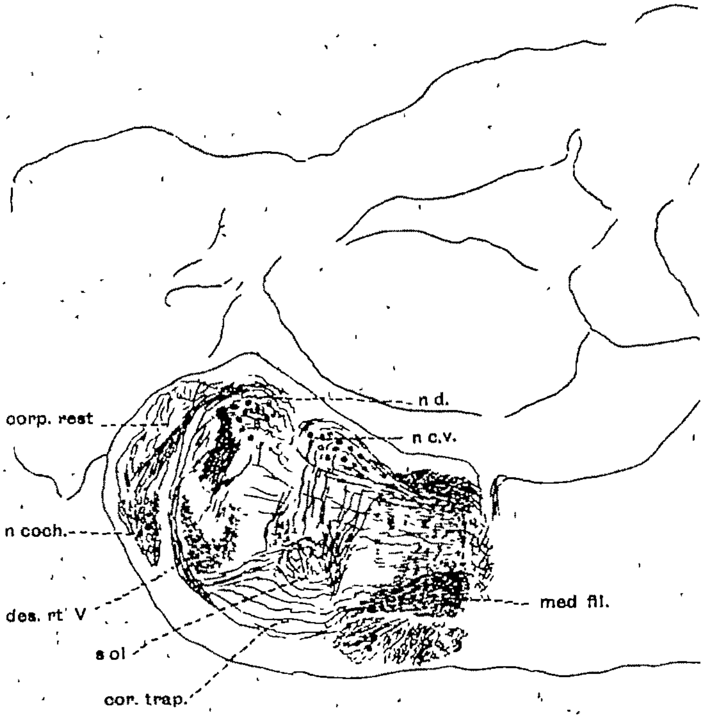

n d.
corp. rest
n c.v.
n coch.
med fil.
des. rt V
s ol
cor. trap.

FIG. 7.

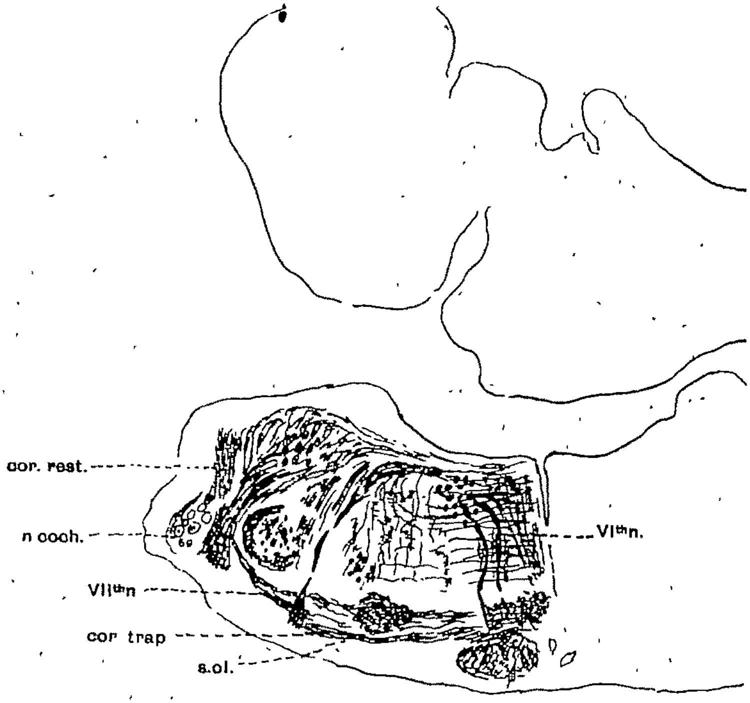
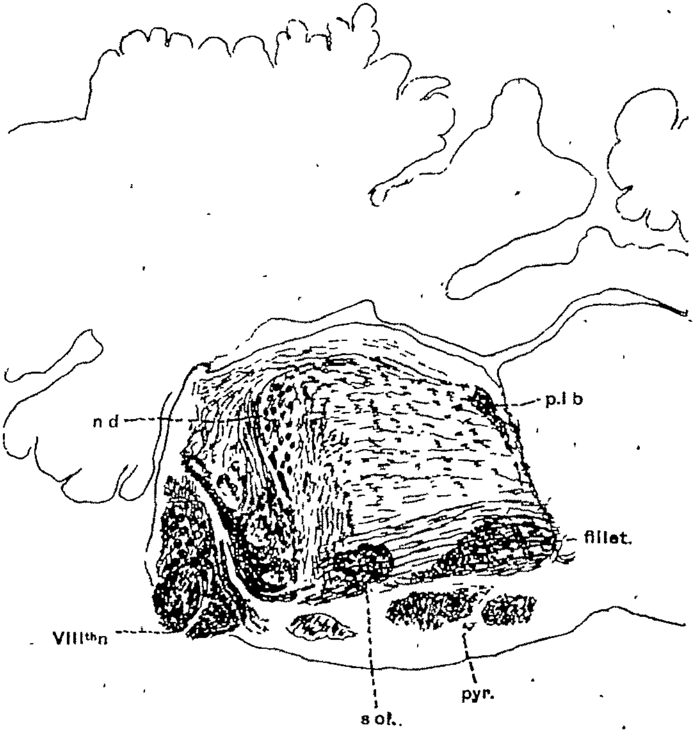

cor. rest.
n coch.
VIIth n
cor trap
s.ol.
VIth n.

FIG. 8.


n d
p.l b
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VIIIth n
s ol.
pyr.

FIG. 9.

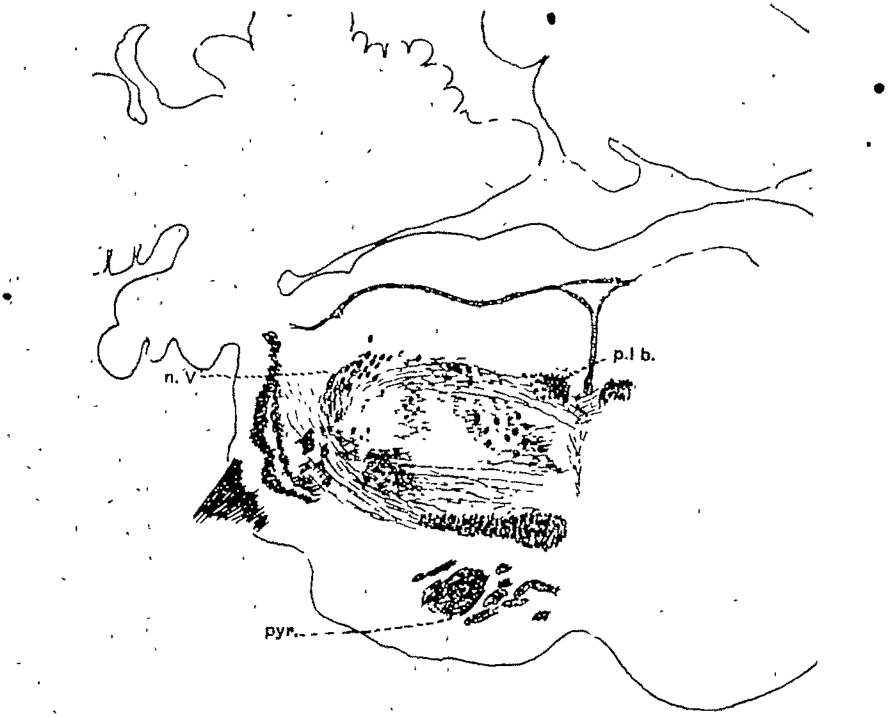

p.l b.
n. V
pyr.

FIG. 10.

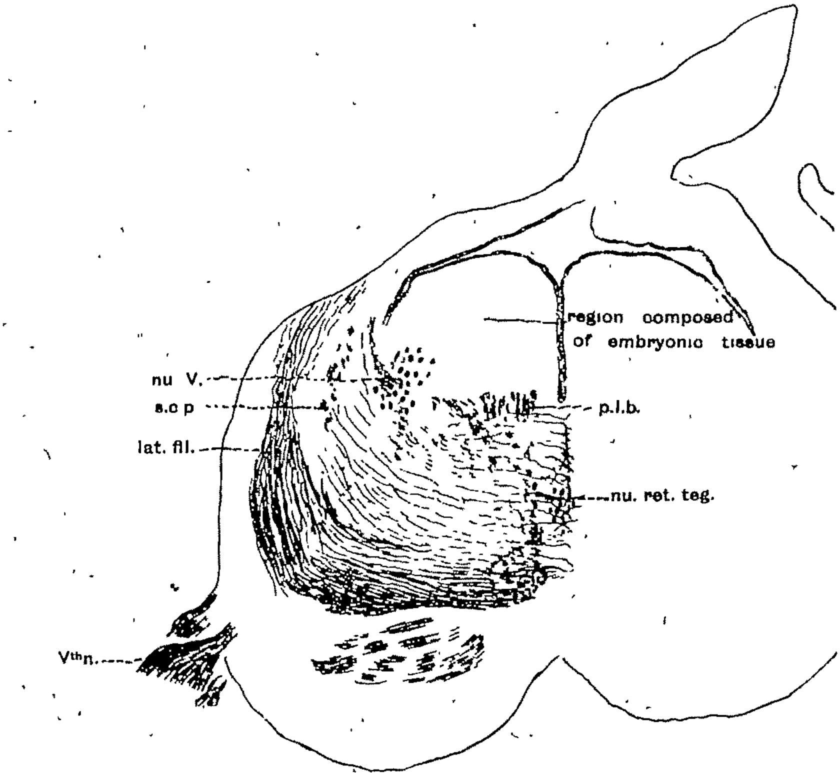

region composed of embryonic tissue
nu V.
s.c p
p.l.b.
lat. fil.
nu. ret. teg.
V^th n.

FIG. 11.

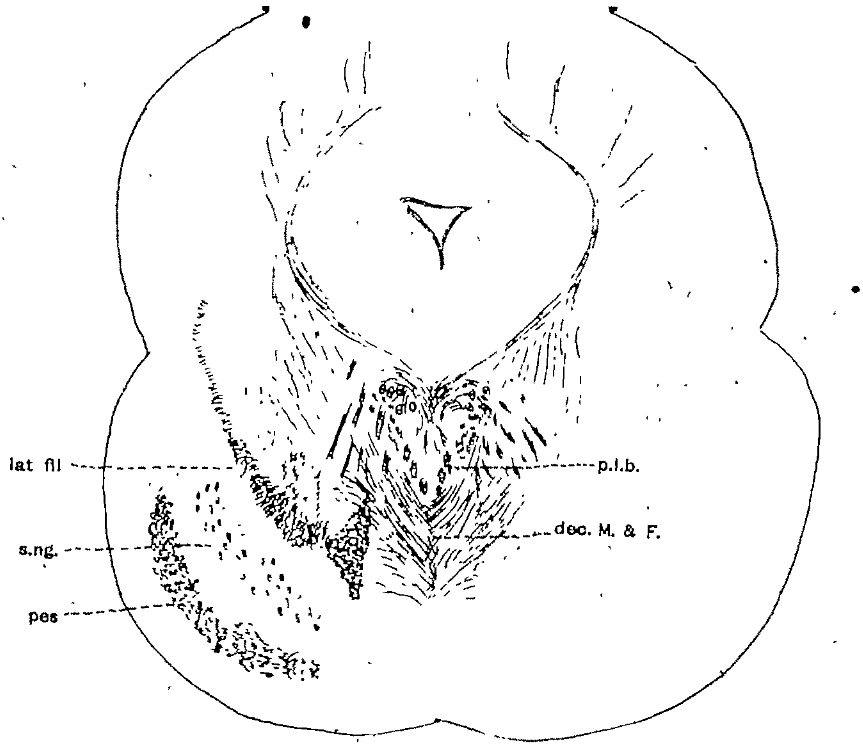


Fig. 12.

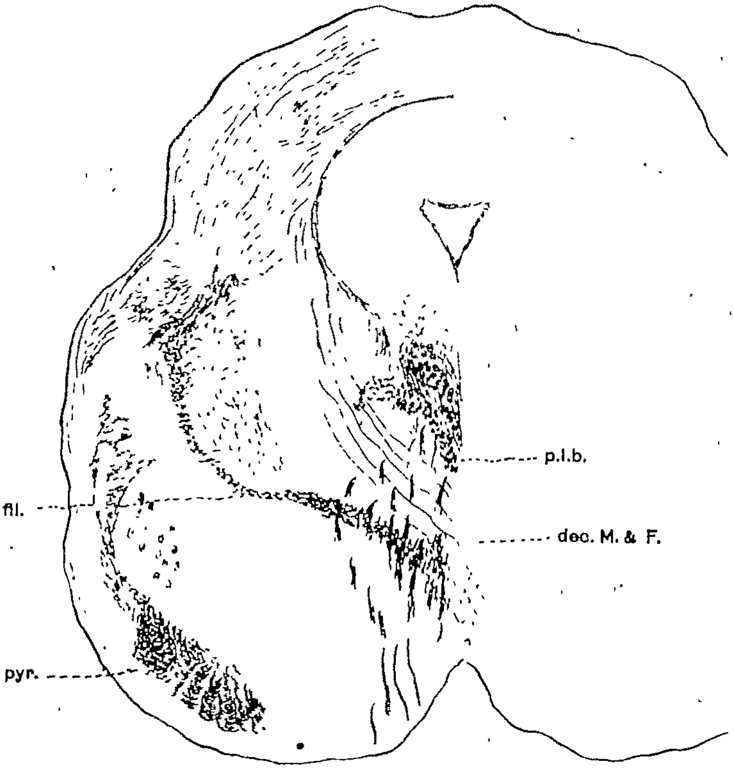


Fig. 13.

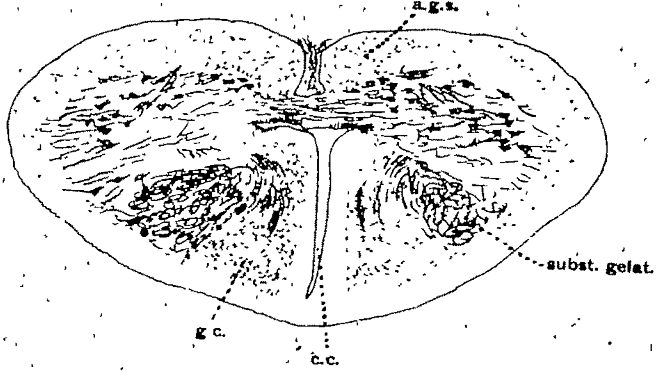


FIG. 14.

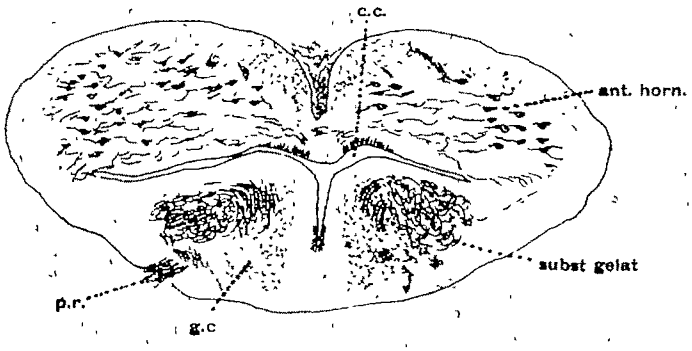


FIG. 15.

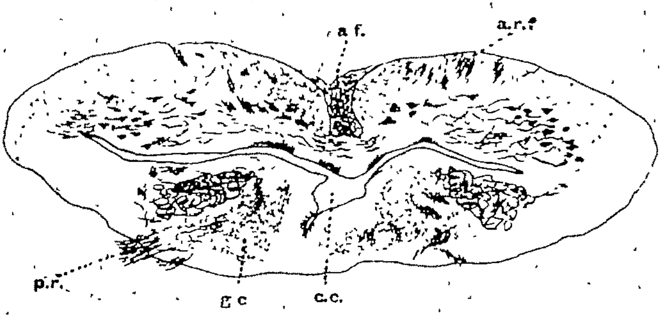


FIG. 16.

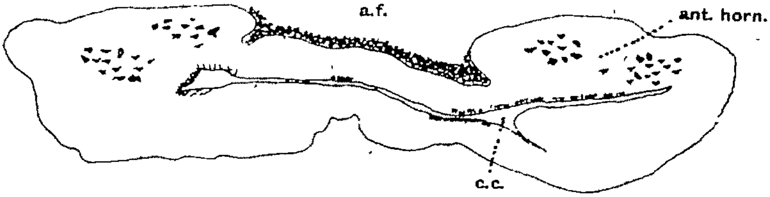


FIG. 17.

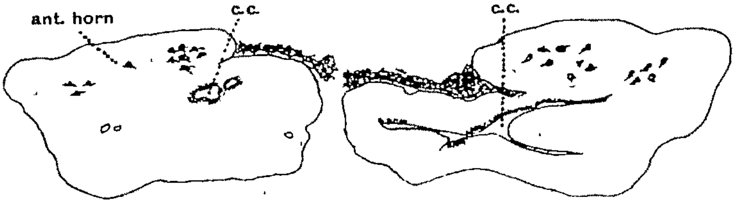


FIG. 18.

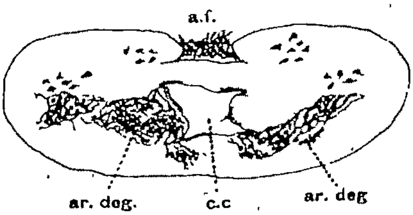


FIG 19.

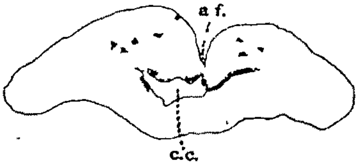


FIG. 20.

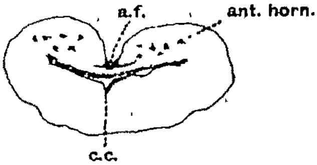
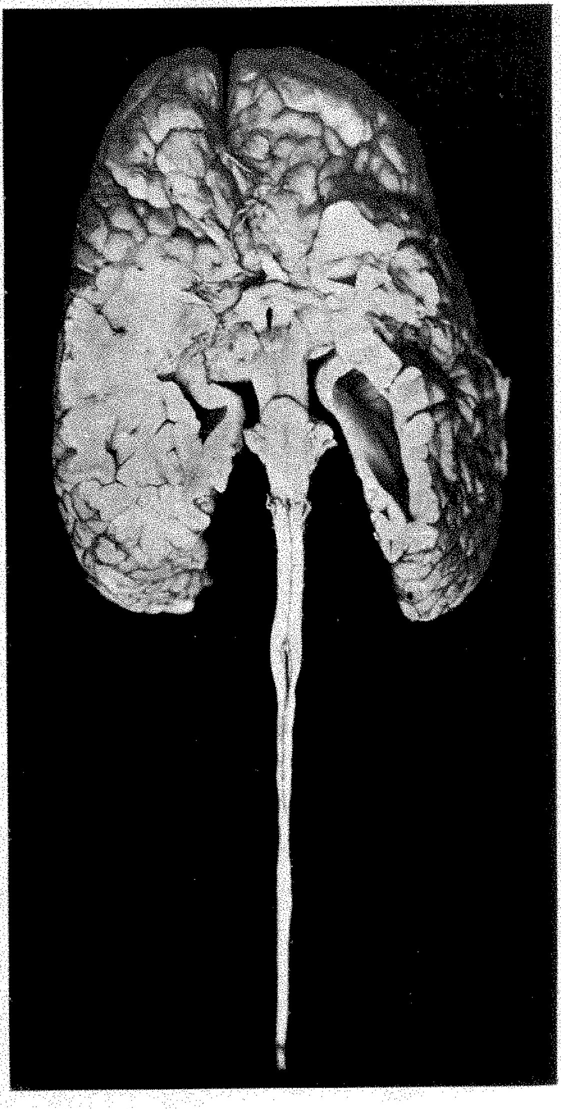


FIG. 21.

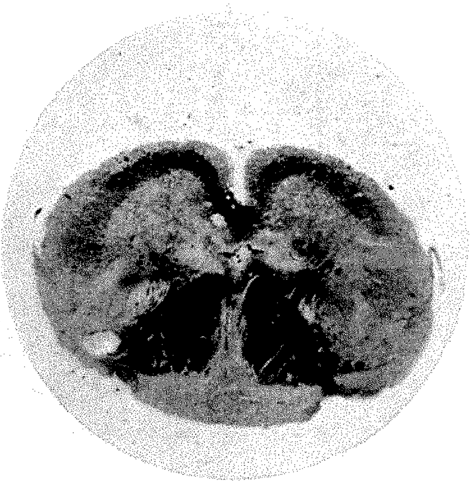
PLATE I.



Anterior view of brain and spinal cord.

To face page 478.

PLATE II.



Photograph at the level of second cervical segment.

To follow Plate I.

TOXIC DEGENERATION OF THE LOWER NEURONES SIMULATING PERIPHERAL NEURITIS.

BY STANLEY BARNES, M.D., B.Sc., M.R.C.P.,
Senior House Physician to the National Hospital for the Paralysed and Epileptic, Queen Square.

THE cases recorded in this paper present a clinical picture similar in many respects to what is met with in peripheral neuritis, and yet in other ways resembling progressive muscular atrophy. I have been able to collect together seven instances[1] of this condition which have recently come under observation at the National Hospital, and I am indebted to Dr. Buzzard, Dr. Bastian, Sir William Gowers, and Dr. Ferrier, for their kind permission to publish these cases.

Case 1.—Lizzie B., a domestic servant, aged 21, was admitted to the National Hospital, Queen Square, on December 18, 1892, complaining of difficulty in walking and weakness of the hands for three and a half years. The family history was unimportant. Although she said she had always been a delicate child, her only previous illnesses had been measles in childhood, and anæmia since the age of 14; the latter had persisted with varying severity up to the onset of the present illness.

In the spring of 1899 she was in bed for a fortnight with rheumatic fever; the attack was a slight one, and in a few days she was about again doing light house work. A week after getting about, she found that the right hand was beginning to get weak, and that the fingers would go blue and cold. The weakness slowly increased, and shortly afterwards began to appear in the left hand, whilst her walking also became impaired. By June, 1899, she had to give up her work, and by July, 1899, the weakness had become so great that she was obliged to take to her bed. The weakness still increased, and for four or five weeks (August, 1899) she lay in bed unable to feed herself, with difficulty in swallowing and in speaking. Bed-sores and incontinence of urine and fæces came on, and a hectic temperature was recorded; delirium was present at times. From this point forwards (September, 1899) she began steadily to improve. She recovered control over her sphincters, swallowing and speech became natural and the bedsores healed. By May, 1900, she had sufficiently recovered to be able to walk with assistance, and to feed herself; since then she has slowly but steadily improved. Whilst at her worst the limbs were absolutely helpless, and very tender, although quite numb; the subjective sensory signs had been absent for about a year before coming into hospital.

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[1] Whilst this communication was in the press, Case 3 died in hospital; the results of the autopsy are reported in the appendix to this paper.

On admission she was a fairly well-built healthy looking girl, with no sign of visceral disease. Her memory was good and she was not emotional. There was no impairment of function of any of the cranial nerves, and the pupils reacted well to light. The muscles as a whole were well developed, especially the trunk and proximal limb muscles. In the arms the extensors and flexors of the elbows were of fair strength, but the extensors of the wrist were markedly weak and atrophic; the flexors of the wrist were also weak, but not so weak as the extensors. Most marked, however, was the great atrophy and weakness of the small hand muscles, especially on the right side; the thenar and hypothenar eminences had almost disappeared, and no faradic or galvanic excitability could be obtained here or in the lumbricales or interossei. The hands adopted the *main en griffe* position, but this could easily be reduced on manipulation.

In the lower extremities, the small muscles of the feet and the anterior tibial muscles were considerably atrophied and almost powerless; no reaction to faradism could be obtained in either set of muscles; the calf muscles were of only moderate power, not nearly so strong as they should have been in a girl of her build; the extensors and flexors of the knee were stronger but probably deficient, whilst hip movements were well performed. The weakness was almost completely symmetrical in both upper and lower extremities, but in both the right limbs tended to be more severely affected.

Slight tenderness of the calves on pressure was the only sensory sign present. Both feet were purplish-blue in colour and were usually very cold; the toe-nails were ribbed and atrophic (since the illness). The skin over the fingers was glossy and smooth, and usually moist with perspiration.

The jerks in the arms were normal; the knee-jerks were present, but diminished; the ankle-jerks were absent on both sides, and the plantar reflexes were difficult to obtain, but of the flexor type. Romberg's sign was absent. The gait was of the "dropped foot" type, without any ataxia.

There was a slight bluish line on the gums opposite several teeth, and of the kind usually seen in cases of lead poisoning; but no history of any lead poisoning could be obtained, nor had she ever suffered from colic. Alcoholism and diphtheria were also definitely excluded.

Under treatment she slowly improved, the forearms and legs especially recovering; the hand and foot muscles showed only slight recovery after a five months' course of massage and galvanism.

Case 2.—Emily G., a single woman, aged 28, was admitted to the National Hospital on August 10, 1900, complaining of weakness of the hands and of the left foot since April, 1900. Her family history was unimportant. She had been a laundress for several years, and had suffered much from indigestion, but had never suffered from any acute disease. Alcoholism was denied.

For a month before the onset of the weakness she had suffered from a moderately severe attack of rheumatism in both feet—pain and swelling at the ankle-joints being the most marked signs. One morning, as the rheumatism was subsiding, she woke up to find her right ankle and left hand weak, and the weakness continued to increase for a few days, until it was as severe as when she was admitted.

On admission she was a well-built woman of good intelligence, and presenting no signs of alcoholism. The cranial nerves, viscera, and sphincters were all normal.

Motor system.—The trunk muscles were well developed and of good power. There was great weakness of the movements of the upper extremities, chiefly in the hands and wrists (extensor movement being weaker than flexion); the elbow movements were weak, and the shoulder movements, though stronger, were evidently below their normal strength. The arms were affected almost symmetrically, but the right was throughout a little the weaker. In the lower extremities there was great weakness of all movements at the right ankle, where dorsiflexion was almost nil. The left leg was affected, but to a much slighter degree. All the limb muscles were flabby and wasted; the small muscles of both hands were almost completely atrophied, the hand adopting the *main en griffe* position; there was much wasting of the extensor group of the forearms and of the anterior tibial group of the right leg. There were no contractures.

Of sensory changes, numbness of the hands and fingers and tenderness of the calves and legs were well marked; there was also slight but definite anæsthesia to light touches and to pin-pricks on both hands. There was well-marked sweating and congestion of the hands and feet.

Electrically, no faradic response could be obtained in the severely atrophied muscles, which required a strong galvanic current to produce a contraction; there was no polar change.

The knee-jerks were present, the left being brisk and the right considerably diminished. There was no ankle clonus, and the plantar reflexes were absent.

She was treated by massage and galvanism to the limbs, and strychnine hypodermically.

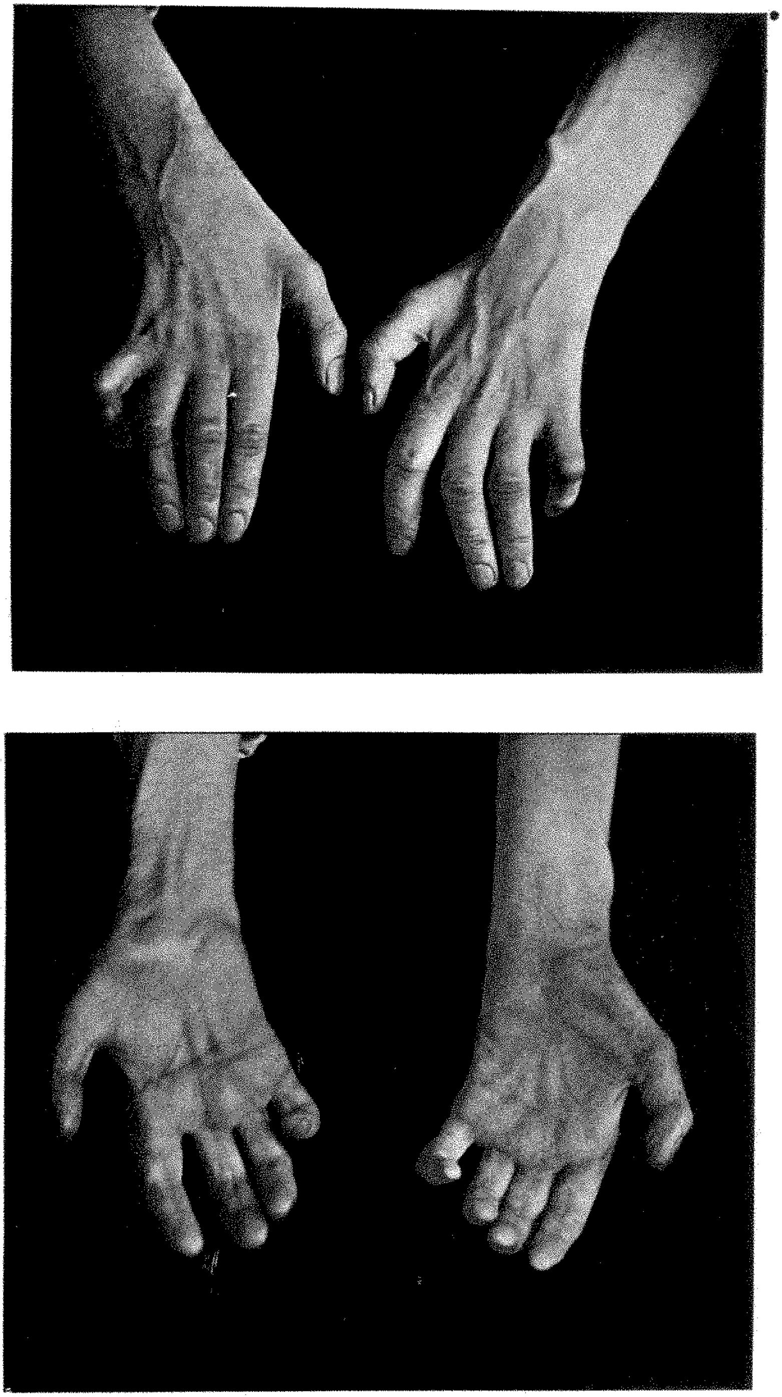
During her six months' stay in hospital she improved greatly in every respect, the hand atrophy and some weakness of flexion of the right ankle alone remaining on her discharge.

Case 3.—Elizabeth A., aged 34, was admitted to the National Hospital on September 8, 1902, complaining of weakness of hands and legs for thirteen months. She is unmarried and her family history is good. In childhood she suffered from scarlet fever and whooping cough, and at the age of 29 she had an attack of "jaundice." Shortly afterwards she went to South Africa, and remained there till a few weeks ago. In July, 1901, she was taken ill with mumps, which ran a fairly usual course; before she was fully convalescent jaundice with headache and vomiting came on, and it was as the jaundice was clearing up that she first noticed weakness of the legs with pain and tenderness of the feet, calves and knees. This got steadily worse, so that in about a month (September) she was unable to stand, and again took to her bed. The condition now began to improve, but a relapse occurred early in November, in which the hands as well as the legs got steadily weaker. She was at her worst about Christmas, 1901, and then had great weakness of the hands with much atrophy of their muscles, considerable weakness of the forearms and some of the upper arm groups; foot movements, especially flexion of the ankle, were much weakened, and all other leg muscles were affected, whilst the trunk muscles became so weak that she was unable to sit up in bed without support. There were no ocular, bulbar, or sphincter troubles.

From that time she slowly began to recover, the trunk muscles first, and then the proximal limb muscles; but the hands and feet have recovered very slightly if at all.

She is a life-long total abstainer, has never had ague, and has

PLATE I.



Case 3.—Very severe atrophy of all the small muscles of the hands on both sides; tendency to the "claw-hand."

never been exposed to lead poisoning. There was no beri-beri in the district.

On admission she was a thin, pale, well-educated woman of 34; her memory was good, and she was not at all emotional. An enlarged movable kidney on the left side was the only visceral abnormality found. The cranial nerves were normal, and there was no optic atrophy or neuritis.

Her muscles as a rule were poorly developed, and could be easily examined owing to the small amount of subcutaneous fat present. The trunk and proximal limb muscles were of normal power and size, but the forearms and legs showed great muscle wasting and weakness, especially marked in the extensors of the wrists and the flexors of the ankles. The wasting here, however, was quite over-shadowed by that of the hands and feet, where hardly any muscle tissue seemed to remain. The hands adopted a *main en griffe* position, but were quite easily passively moved; the only muscle that could be felt to contract in either hand was the abductor transversus pollicis.

The feet were "dropped" but flaccid, not contractured; they could just be flexed against gravity; all the intrinsic foot muscles seemed to have disappeared; no faradic excitability could be obtained in the feet or hand muscles.

There was a sense of numbness of the hands and fingers and of the feet and toes, but no objective sensory change could be demonstrated here. The skin of the hands and feet was smooth, glossy and perspired freely, but the nails were normal. She could only walk with assistance—a typical "dropped foot" gait.

Up to the present (September 28) no material change has occurred in the condition.[1]

Case 4.—Ellen H., a domestic servant, aged 36, was admitted to the National Hospital on April 1, 1902. She complained of weakness of hands and legs of eight months' duration. The family history was good, and her own health had been good except for an attack of rheumatic fever at the age of 14.

In September, 1901, she had an attack of diphtheria; the attack was of moderate severity, and the local signs soon passed off. About three weeks after the onset of the diphtheria, she noticed her speech was becoming nasal, although she never had regurgitation of fluids through her nose; at the same time double vision and considerable difficulty in reading came on, quickly followed by a sense of heaviness of the hands and feet, the right hand and the left foot being chiefly affected.

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[1] See Appendix.

There was at no time any sphincter trouble. As far as can be ascertained, the weakness of the hands and legs progressed for about eight weeks; certainly no improvement began to occur until March, 1902, or about four months after the onset of the paralysis.

Thenceforth a slow but steady improvement occurred, the left hand and the right leg especially improving.

With the paralysis had come on pain and great tenderness of the legs, and to a less extent of the forearms; whilst numbness and difficulty in distinguishing objects touched by her hands had also been very marked, but were considerably improved.

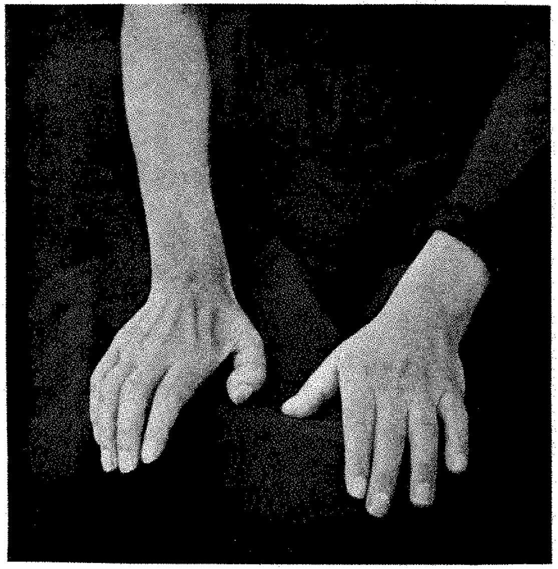
Atrophy of muscles began to come on shortly after the onset of the paralysis, and became progressively worse until Christmas, 1901. By this time the small muscles of the right hand were extremely atrophic, those of the left being less so, but still markedly smaller than normal. The forearm and legs were also much wasted, and some general emaciation had also occurred.

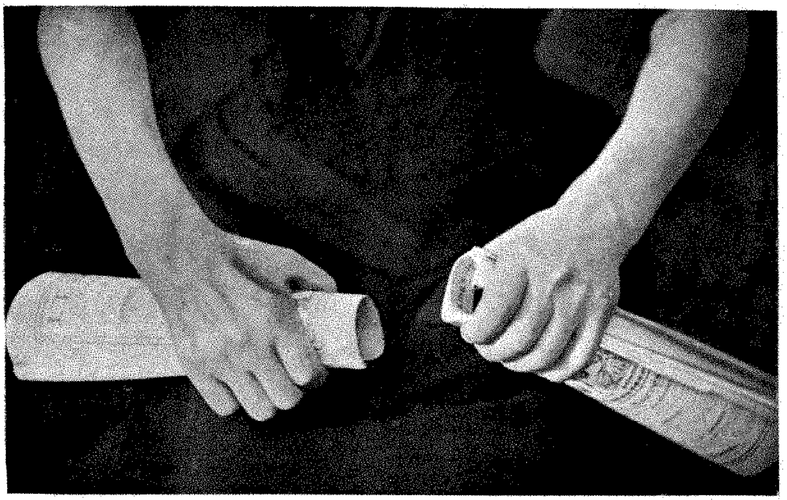
The atrophy remained unchanged till March, 1902, since which a steady filling out of the muscles had occurred, only the right hand muscles now being severely wasted.

On admission, she was a fairly well-built woman of healthy appearance; no abnormality was detected in the thoracic or abdominal viscera. The muscles generally were of good size and power, but there was considerable wasting of the forearm and legs (below the knees especially), and the small muscles of the right hand were extremely atrophic; the left hand muscles were also atrophic, but to a much less extent than those of the right hand. In the latter the interossei, abductor pollicis, flexor brevis pollicis and opponens had almost disappeared, and no faradic or galvanic irritability could be found in them. In each forearm the extensors were weaker than the flexors, but both sets of muscles reacted to faradism; it was also noticeable that the wasting was greater on the ulnar than on the radial side of the forearm, and that in firmly grasping an object with her right hand, the hand was not only slightly flexed on the forearm, but was also deflected to the radial side (see photograph, Plate I.). In the left forearm and hand similar changes were also visible, but were much slighter. By September 25, 1902, when the photograph was taken, the left forearm and hand were practically normal, and contrasted markedly with the still atrophic, though also improved, right forearm and hand.

In the lower extremities "foot-drop" was well marked, especially on the left side, and there was corresponding wasting and diminution of faradic excitability of the extensor groups of the

PLATE II.





CASE 4.—The upper figure shows the marked atrophy of the right hand muscles as compared with the left. The lower figure shows the position of the hand in grasping, *i.e.*, slight flexion at wrist with deflection to the radial side.

legs; the small muscles of the feet were very atrophic, especially on the left side; there was very slight contraction of the calf muscles.

Movements at the elbows and knees were all of moderate power, whilst those of the shoulders and hips, as well as all trunk movements, were of normal strength. The ocular, facial, palatal, mandibular and lingual muscles all appeared to act perfectly.

Anæsthesia to all forms of sensation existed markedly on the right hand and wrist and upon the left foot and outer side of the leg below the knee. None could be made out on the left hand and right foot, although in these members also the patient had a subjective sense of numbness. Of the reflexes the supinator jerk was diminished on the right side, but normal on the left; both knee-jerks were rather brisk, but no ankle-jerk could be obtained on either side; the right plantar reflex was of the flexor type, but the left was absent. All the other reflexes were normal. Both hands and both feet were nearly always blue and cold, and sweated profusely.

Under treatment by massage and galvanism, slow but steady improvement has occurred, so that now (September 28) the left upper extremity is almost normal, and much improvement has taken place in the right arm and hand; foot-drop is still present to a slight extent on the left side, but is far less marked. The objective anæsthesia has almost entirely disappeared.

Case 5.—Mary H., a single woman, aged 39, was admitted to the National Hospital in September, 1899, complaining of general weakness and loss of power. There was a strong neurotic history on her father's side, one uncle having suffered from alcoholic insanity and two others from neurasthenia; her mother was suffering from Bright's disease. The patient had always been of a "nervous temperament," and had had much domestic worry of recent years. For a considerable time before admission she had been a housekeeper, and had taken two bottles of stout a day; recently she had had frequent toothache, for the relief of which she took whisky, sometimes as much as eight glasses a day.

About Christmas, 1898, she took a long drive and caught a chill; she found that on her return home her hands were weak and her legs were less steady than usual. Since then the weakness had steadily increased, and slight numbness had come on in the extremities. Cramp pains in arms and legs had been frequent, but no other pain was complained about.

The limbs wasted considerably, especially the upper extremities, so that by September, 1899, although she could still walk, she was unable to button her clothes, &c.

There was a history of some mental enfeeblement and occasional hallucinations during the two months prior to entering the hospital.

On admission she was a moderately wasted woman of good colour. Vision was good and the optic discs were normal. The pupils reacted well to light and on convergence the other cranial nerves were also normal. The muscles as a rule were of poor size, more especially those of the limbs. Trunk movements were of good power and those at the shoulders, elbows, hips and knees were also fairly good. The forearms were considerably weakened and wasted, the extensors of the wrist and fingers having suffered more than the corresponding flexor muscles, although the latter were obviously weak. The small muscles of the hands were greatly weakened and wasted, and were by far the most atrophic muscles found; the lumbricales and interossei had been affected as much as the thenar and hypothenar groups; some fibrillary twitching was to be seen in the thenar muscles. The affection of the legs was comparatively slight, the flexors of the ankle not being markedly more weakened than the extensors. The gait was feeble and shuffling, but not of the "steppage" type. There were no rigid contractures.

Of sensory changes, numbness in the hands and feet were present to a slight degree only, but no definite loss of sensibility to light touches or pin-pricks could be found.

The muscles of the legs and arms were slightly tender if squeezed. There was no sphincter defect. The tendon jerks were present in about the normal degree in the upper and lower extremities and were equal on the two sides. The jaw-jerk was present, and the plantar reflexes were of the flexor type.

The only electrical changes found were in the small muscles of the hand, where a well marked reaction of degeneration was present.

The patient was treated in hospital for about six weeks by massage and galvanism, but no material change in the condition had occurred on her discharge.

Case 6.—Henry N., a sea captain, aged 50, was admitted to the National Hospital on November 1, 1897, complaining of weakness of the hands and legs.

His previous history was good, except that he had been constantly exposed to cold and wet (once having been shipwrecked) and had suffered from erysipelas of the scalp eleven years previous to admission. He was a total abstainer from alcohol, and had never had malaria or any other fever.

About March 1897, he had an acute febrile attack with a temperature of 103°, for which he was admitted to hospital. He was at first supposed to be suffering from enteric fever, but in three or four days the temperature fell to normal and remained so. He was kept in bed for five weeks, and during this time the left leg became gradually weak, quickly followed by a progressive weakening of the hands and right leg; some general wasting also occurred, but there was at no time any difficulty with swallowing or with speaking; the sphincters were unaffected. There was no loss of feeling anywhere.

On admission six months after the onset, he was a powerfully-built man, of good memory. There was no defect of any of the cranial nerves.

There was a great wasting of the interossei, thenar and hypothenar eminences of both hands, more marked in the right than the left; there was also considerable wasting and corresponding weakness of the muscles on the ulnar side of the forearms. The long extensors and flexors of the fingers were weak, but all other muscles in the upper extremities were of good size and power. In the lower extremities there was some atrophy of all the muscles below the knees, and considerable weakness of the calf and anterior muscle groups. The gait was feeble and of the "dropped-foot" type.

The electrical reaction showed nowhere a full reaction of degeneration, but in the weakened muscles there was a diminished excitability to faradism. The supinator-jerks and knee-jerks were equal on both sides and normally brisk; but no plantar reflex or ankle-jerk was noted. No objective sensory changes could be made out.

The patient remained in hospital for three months, during which time no further progress of the disease occurred. He was discharged on February 1, 1898, in a slightly improved condition.

Case 7.—George G., an engineer, aged 22, was admitted to the National Hospital on April 18, 1899, complaining of weakness in the arms and legs of nine months' duration. The family history and previous history were good; he had never taken alcohol, nor had he suffered from ague or tropical fever.

The onset was rather acute whilst he was apparently in good health, and off the Coast of Mauritius. His first symptom was weakness in the right hand, and this was quickly followed by weakness in the left hand and difficulty in walking. The weakness rapidly increased, and in a few days both upper extremities were weak in all their movements, and he became unable to stand. There was severe pain and tenderness in the legs, especially at night-time, there was never any feeling of numbness, nor any sphincter trouble. He was taken into hospital a few months later and improved whilst there, but on his discharge the weakness again increased until he was admitted to the National Hospital six months after the first sign had occurred.

On admission, he was a well-built young man of fair education. The abdominal and thoracic viscera appeared to be healthy, and no defect was found in the cranial nerves. Motor power was good in the trunk and shoulder muscles, but extension and flexion of the elbows were below normal strength. Flexion of the wrist was weakened, but not so much as extension; all the movements of the hands were very weak, but none were lost. There was marked atrophy of the thenar, hypothenar and interosseous muscles in both hands, and to a less extent there was wasting of the forearm muscles.

In the lower extremities dorsiflexion of the ankle was his weakest movement, and the calf muscles were also considerably weakened; other movements were of good power. There was considerable tenderness of the calves on pressure, and great pain was caused by pressure over the nerve-trunks. There was no objective anæsthesia. The knee-jerks were normal, and the plantar reflexes were present and of the flexor type.

He remained in hospital for three months, being treated by massage and galvanism; he steadily improved, and on his discharge he had almost completely recovered, only a little weakness and atrophy of the hand muscles remaining.

CLINICAL CONDITION.

At the stage when they came under observation the cases recorded above all showed a well-marked atrophy of the small muscles of the hands, together with weakness of the extensors of the wrist and of the flexors of the ankle. The atrophy of the small muscles of the hand in five of the cases reached a severe degree, and especially in Case 3, where only the slightest contractions were possible in the interossei, lumbricales, thenar, or hypothenar muscles. In the more severe cases there was no reaction to the faradic current in the hand muscles, and diminished reaction in the extensor group of the forearms and in the flexor group of the ankle. In other words, there was an atrophic paralysis of the peripheral type, a paralysis in which the most distal muscles had suffered severely, and in which the proximal muscles were only slightly or not at all affected. In none of the cases did the muscles particularly affected correspond to particular peripheral nerves; the distribution of atrophy corresponded rather to the segments of the cord, the first dorsal supply being especially picked out.

A marked feature of these cases was the absence of rigid contractures. The reason for this appeared to be twofold: firstly, because there was little or no pain on active or passive movement, so that the limbs were kept constantly supple; and secondly, because with the severe atrophy and loss of power of particular muscles there always occurred weakening of the neighbouring muscles.

In all the cases sensory changes, though present, were comparatively slight. They were most marked in Case 4, in which patient definite objective anæsthesias could be made out. All but one of the patients complained of *numbness* in the extremities at some period of the disease, but, as a rule, this sensation was only temporary, and was not noted after admission to hospital. The most prominent sensory sign in all the cases was *muscle tenderness* and tenderness on pressure over the nerve-trunks in the limbs; this persisted in every case until admission, although in Case 1 the most severe grade of the disease had occurred some three years previously. The sensory changes found were thus similar in all respects to those seen in ordinary alcoholic neuritis, but were much less severe at all periods of the disease. In none of the cases was any change found in the fundus oculi.

Case 1 was the only case in which sphincter trouble had occurred; bulbar signs also only occurred in this case at its worst stage and in the case which followed diphtheria, so that, apart from the well-known selective action of the diphtheria toxine in paralysing the palate and ocular muscles, it might be said that cases of the kind recorded here do not show signs of involvement of the cranial nerves, except in those instances in which a severe and widespread paralysis exists.

Diagnosis.

None of the cases were seen during the progress of the acute symptoms in the early stages. Had they been seen then, there is little doubt that the diagnosis would have been very difficult and that they would have been called multiple neuritis, Landry's acute ascending paralysis, or possibly polio-myelitis. The rapidity of onset of the nervous symptoms was extremely variable, varying from a few days (as in Case 7), to nearly seven months (as in Case 1). With regard to the acute cases, the resemblance to Landry's paralysis, must have been extremely striking—the rapid spread of paralysis from the periphery to the central muscle groups, the slight sensory signs, the slight involvement of the sphincters and the absence of tendency to the formation of bed-sores. In none of the cases recorded was I able to get any account of the electrical excitability of the muscles in the early stages. From the histories given, atrophy of muscle appeared only to come on late in the disease and would not, therefore, assist in the diagnosis at an early stage.

The diagnosis from pure acute or sub-acute polio-myelitis would have been less difficult in the early stages, owing to the sensory signs present. All the cases gave a history of muscle tenderness, and in most of them numbness of the extremities, a sensation of tingling or (spontaneous) pain in the limbs were present, and from the patients' accounts were much more severe and persistent than is usually seen in acute anterior polio-myelitis. The distribution of the paralysis would also have given a clue to the character of the disease in most cases, for although the signs were as a rule mainly motor, there was a well-marked symmetry of affection both in the upper and lower extremities, which would strongly suggest rather a general toxic or inflammatory condition than a focal polio-myelitis. The fact of the disease occurring in adults would not of course of itself negative a diagnosis of acute polio-myelitis.

Later in the disease, particularly at the stage when the cases were seen in hospital, the diagnosis was in several cases a matter of considerable difficulty at first. It looked as though we had to deal with a patient who had suffered from some acute paralytic condition upon which had been grafted as it were a chronic progressive muscular atrophy. Certainly the resemblance to the Aran-Duchenne type of the latter disease was very striking—the claw hand with atrophy of hand muscles which showed the electrical changes of degeneration, with more or less definite atrophy of other muscles, almost exactly resembled what is seen in progressive muscular atrophy; but the diagnosis of this disease in association with an old neuritic condition was clearly negatived by the course of the affection and the regularity with which one or both of the knee-jerks was found impaired or lost. It is almost unknown in the Aran-Duchenne form of progressive muscular atrophy, to meet with a patient whose knee-jerks are not brisk, except in association with definite atrophy of the quadriceps muscle. In none of the recorded cases was there such a definite atrophy, and in none was there any exaltation of the tendon jerks in the lower limbs; ankle clonus was never found, and the plantar reflex was usually deficient or absent, and when present was always of the flexor type. In only one case also was there any contracture of the calf muscle, and even here (as in the other cases), the lower limbs were quite flaccid. The course of the disease was even more certain evidence that the condition was not one of progressive muscular atrophy. Despite the great wasting of muscles that had occurred in some of the cases, all the patients under observation tended gradually but constantly to improve. Even the hand muscles have filled out again after appearing almost absent, as has been especially noticed in Case 4 during the six months she has been under observation.

The diagnosis of multiple neuritis could not be excluded in any of the cases. In each of them there was the same type of atrophy and weakness with muscle-tenderness, largely symmetrical in distribution and with diminished tendon-jerks. The most marked differences from the usual form of polyneuritis were—(1) the great atrophy of the intrinsic muscles of the hands; (2) the comparative slightness of sensory changes; (3) the absence as a rule of contractures and (4) the integrity of the psychical condition.

Prognosis.

In all the cases at the stage at which they first came under observation, the prognosis was good in that they tended constantly to lose their sensory signs and to gain power in the affected muscle groups. The hand muscles appeared to be the last to recover, and as far as it has been yet possible to trace the cases, it would seem that years may elapse without full recovery occurring. Nevertheless in all the cases a steady if slow improvement was the rule. In only two of the seven cases was there a history of anything approaching a relapse; all improved under hospital treatment.

Etiology.

Five of the cases gave a history of some febrile condition preceding the onset of the disease, viz., rheumatism (in two cases), diphtheria, mumps, and some pyrexial disease of unknown origin in one case each. In one a definite history of alcoholism was found; in the last case no etiological factor could be made out. As compared with the peripheral neuritis usually seen, it is remarkable that only one of the seven cases might be of alcoholic origin; it is also worthy of note that all of the above factors have also been recorded as antecedents of Landry's paralysis. The severity of the antecedent disease does not seem to have been at all commensurate with the degree of weakness following; for example, in Case 1 the attack of rheumatism was extremely slight, whilst the paralysis ultimately became very severe.

Pathology.

In none of the cases did a fatal termination ensue,[1] so that the morbid anatomy and pathology can only be inferred from clinical considerations, and from a comparison with what has been found in similar but fatal cases. Regarded from a purely clinical standpoint it is difficult not to conclude that we are here dealing with a disease which has affected not only the peripheral nerves but the spinal cord. Referring to progressive muscular atrophy, Gowers (1) states that "cases are met with (although not frequently) that present every gradation to subacute polio-myelitis in one direction, and perhaps also to polyneuritis in another." Clinically, the cases reported here appear to be of this intermediate form. If the severe atrophy of the hand muscles (as shown in the photographs) is to be considered as solely a pheripheral nerve lesion, then it must be that particular parts only of peripheral nerves are involved, for the atrophy is as severe in those hand muscles supplied by the median as in those supplied by the ulnar nerve, whilst many muscles of the forearm supplied by the median have remained of fair power. It seems much more rational to suppose that we have here to deal with a toxic affection of the lower neurones, the motor neurones being much more severely affected than the sensory.

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[1] See Appendix.

On this hypothesis it would be comparatively easy to understand why a mixed motor and sensory nerve like the median should have lost some of its functions whilst others remain. For we should then be dealing with a kind of system degeneration, in which the fibres supplying the muscles subserving the more highly organised movements in the upper extremities are the ones which suffer first and most. We are, however, bound to assume also that the toxine, or more probably toxines, do not act solely on the lower motor neurones, but also upon the lower sensory neurones, although to a much slighter degree; otherwise it is impossible to explain the symptoms of persistent muscle-tenderness, numbness, and anæsthesia which have been noted. This view of the pathology of these cases accords well with the findings of Batten (2) in cases of diphtheritic paralysis; he found "that the dominant lesion in diphtheritic paralysis is a parenchymatous degeneration of the myelin sheath of the nerves. . . . It seems almost certain that a general poison like that of diphtheria must act on the whole neurone, and . . . that the effect of the poison manifests itself at least in fatal cases in the myelin sheath, and not in the cell-body." However true it may be that in ordinary forms of diphtheritic paralysis there is no change in the cell-bodies, yet it is difficult to believe that cases like those recorded here with long persistent local atrophies are due purely to peripheral nerve affections.

A case very similar to these was published this year by Luzzetto (3), in which malaria appeared to be the cause of the paralysis. The patient rapidly developed paralysis of the hand muscles and of the extensor groups of the forearms, with muscle-tenderness, but no objective sensory change; marked atrophy of the thenar and hypothenar muscles followed, and the patient died of pneumonia about two months after the onset of the nervous symptoms. Marked degenerative changes were found in the nerves and in the anterior horn-cells, and Luzzetto concluded that the cord changes were not secondary to the nerve changes, but that the whole neurone was involved simultaneously.

Another case in many respects resembling those under discussion has been published by Stewart (4). The patient was a woman of 33 years of age, and seven months pregnant at the time of the onset of the disease. No febrile attack preceded the illness, and no other toxic cause could be discovered. The symptoms were numbness of the hands and feet, much tenderness of the calves, and some anæsthesia with atrophy of muscles in the upper and lower extremities. The disease progressed for about six months, the patient dying of pneumonia. The nerves here showed both parenchymatous and interstitial changes, evidently a true neuritis. There was also a doubtful inflammatory condition in the capsule around the anterior horn-cells of the cord, and undoubted chromolytic changes, and in places atrophy of many of the cells.

The cases recorded here appear to correspond clinically rather to the first than to the second of these cases, in that, in Stewart's case, sensory changes were very marked, almost if not quite as marked as in cases of alcoholic neuritis. Possibly the reason for this difference in the clinical symptoms is that the first recorded (malarial) case, was one of toxic degeneration and not of true neuritis; whereas in the second case there was a marked inflammatory condition of the peripheral nerves. I think the distinction is an important one, although it is quite likely that the two conditions may be present in a single case. It would appear probable that when the nervous system is suddenly flooded by toxines the full effects of the poison may be developed, and a true neuritis ensue; whereas if the same toxine were only administered in small doses over a longer period, a selective action might ensue, and cause a degenerative as opposed to an inflammatory reaction. It must also be true that certain of the toxines causing flaccid palsies tend rather to produce inflammatory than degenerative results and *vice versâ*; for instance, diphtheria only rarely causes any interstitial inflammation of peripheral nerves, whereas it is almost the rule in the alcoholic palsies to get an interstitial neuritis developed. Toxines like those of influenza, rheumatism, mumps, &c., would appear to approach more closely to the diphtheritic type, *i.e.*, to cause parenchymatous degeneration rather than interstitial neuritis, and it is not surprising to find the symptoms of the "neuritis" following these diseases differing in a more or less marked degree from those seen in the more common (alcoholic) form of multiple neuritis.

At the present time it is impossible to discuss the pathological relationship between these cases and Landry's paralysis. The latter disease is a clinical symptom-complex, and its pathology is as yet uncertain. Raymond (5) considers that polyneuritis, poliomyelitis and Landry's paralysis are diseases that cannot be sharply distinguished from one another, and that they have the same etiology. Redlich, too, believes that polio-myelitis and polyneuritis are the same affection with different localisations. On the other hand, E. W. Taylor (6) denies that there is any certain evidence of a coincident inflammation of the ventral horn and the peripheral nerves.

I am inclined to think the balance of evidence is in favour of a coincident affection of the whole of the lower neurones, possibly more marked in one part of them than another; that in these cases the motor neurone is more severely diseased than the sensory neurone; that in the cases recorded here, there is a parenchymatous degeneration rather than a true inflammation; and lastly, that although at some stages of the disease there is a lesion sufficiently severe to destroy for the time being the functions of the main mass of the nerve-fibres to the limbs, that in great part the lesion falls short of absolute destruction, so that a large amount of repair is possible in all cases, and that in some cases the repair of tissue and consequent recovery of function may be complete.

CONCLUSIONS.

(1) There is a clinical type which is usually the sequel of acute specific fevers, which resembles the paralysis seen in multiple neuritis, but which is associated with great atrophy of the hand muscles. It usually begins about the second or third week after the febrile condition, and involves the muscles from the periphery to the trunk to a varying extent. It may progress for a few days only, or for several months. Sensory signs are present, but slight in degree. Although the condition somewhat resembles progressive muscular atrophy, the prognosis and etiology of the two conditions are probably widely different from one another.

(2) After a certain stage, when once definite improvement has begun, relapses are not common, and there is a constant tendency to improvement. Even years after the subsidence of the acute condition considerable improvement may still take place, the small muscles of the hands being the last to recover. Contractures are rarely developed.

(3) Probably the condition is one of toxic degeneration of the lower neurones, the motor neurones being more particularly affected.

APPENDIX.

A further report of Case 3, with results of *post-mortem* examination.

On November 17, 1902, whilst still in hospital, the patient began to complain of obscure pain in the back and a general sense of uneasiness. Nocturnal restlessness and insomnia came on, and the enlarged kidney became slightly more tender on pressure; there was a light cloud of albumen in the urine. This condition persisted for several days, and on November 24 she complained of feeling much weaker, and was unable to sit up in bed. It was then found that all the tendon-jerks had disappeared since the previous week. Numbness and tingling came on in the hands and feet, and next day there was incontinence of fæces and urine (although she was fully conscious) and respiration was embarrassed. No bulbar signs developed, but she died in the afternoon of November 25, of respiratory failure. The mode of death was almost identical with that which occurred in a case of Landry's paralysis which was in hospital shortly afterwards.

At the autopsy held next day, there was found congenital cystic disease of both kidneys of considerable severity; both kidneys were very much enlarged, but contained so much normal parenchyma that it is almost certain that this was not the direct cause of death. The other abdominal and thoracic viscera were normal. The spinal cord was smaller than usual, and most of the nerve-roots and peripheral nerves originating from the cervical and lumbo-sacral enlargement were thin and wasted.

Attempts to cultivate bacteria from the cerebro-spinal fluid and spinal cord, gave negative results (gelatin, agar-agar and bouillon). The central nervous system was removed and hardened partly in formalin and partly in absolute alcohol, and sections were prepared by the methods of Marchi, Weigert, Nissl and van Giesson; a few sections were also stained by hæmatoxylin and eosin. The peripheral nerves and posterior root ganglia were similarly treated, and parts of apparently normal and diseased muscles were stained by hæmatoxylin and eosin.

The following microscopic changes were found:—

Muscles.—The erector spinæ, infra-spinatus and flexor muscles of the forearm were normal. The pronator quadratus was moderately affected, as were the extensors of the wrist. The lumbricales, flexor brevis pollicis, abductor pollicis, opponens pollicis and hypothenar muscles all showed very marked changes from the normal.

In the diseased muscles there was found great thickening of the arteries and a proportional increase in the general fibrous tissue; in all probability there was no actual increase in the amount of fibrous tissue, the apparent increase being due to wasting of the muscle-tissue. There was no small-celled infiltration. The tendon appeared normal, and the muscle spindles remaining completely unaffected side by side with atrophic muscle-fibres, were very prominent and proportionately numerous ; in every case the muscle-fibres contained in the muscle-spindles remained normal.

Atrophy of muscle-fibres has occurred very diffusely ; in some muscle-groups, it is true, nearly every fibre is atrophic, but the rule is for the degenerated fibres to lie side by side with normal ones. In those muscles which are only partly affected, only certain of the muscle prisms show any atrophic fibres ; in a severely affected muscle (the lumbricales for instance) every prism contains some degenerated fibres. The affected fibres are much reduced in size—to about one-sixth of their normal cross section ; they stain more darkly than usual but preserve their striation perfectly. They are not particularly granular, and contain no fat ; they have not lost their regularity of outline.

Nerves.—The ulnar nerves were the most severely affected of the nerves examined. Hæmatoxylin stained sections showed marked thickening of the coats of the arteries, but no increase in the number of nuclei present nor any proliferation of interstitial tissue. By the Weigert method marked changes were found. Whole strands of fibres were degenerated and showed simply beads of unabsorbed myelin instead of a continuous medullary sheath. Many very finely medullated fibres were seen which showed fusiform swellings of myelin—probably regenerating fibres. About one-eighth of the fibres were of the normal size ; about one-third of the fibres were reduced to about half the normal diameter ; whilst the rest consisted of the very fine fibres with fusiform swellings. As in the case of the muscles, the fibres affected were scattered very diffusely throughout the nerve, and did not lie in special bundles. By the Marchi method no degenerative changes could be made out ; in all probability the fragmentation of myelin seen in some of the fibres by the Weigert method was an artefact.

Posterior root ganglia.—These all appeared to be normal in every respect.

Medulla and spinal cord.—All the sections of the medulla were normal ; no sign of any affection of the hypoglossal or vagus nuclei could be found.

In the spinal cord no abnormality could be detected by the Marchi or Weigert-Pal methods in any of the tracts. Sections stained by the van Giesson method showed an extremely marked change in the vessels of the whole spinal cord ; these changes were most marked in the cervical enlargement, but were also present to a less extent in the lumbar enlargement and dorsal region. A section taken at the level of the eighth cervical segment (where the affection was severe) showed a great thickening of the walls of all the arteries, which appeared to be embedded in a faintly striated material with a peculiarly vitreous appearance; it stained faintly with basic dyes, and bright red with van Giesson's solution, but did not give the amyloid reaction. The septa seemed to be entirely composed of this material, and were greatly swollen; the pia mater immediately around the cord was similarly though less severely affected. Where vessels were cut in cross-section, this material was faintly laminated as it lay around them; a few nuclei were scattered irregularly through it, but otherwise it presented an almost homogeneous appearance. The vessels and supporting tissue of the nerve-roots at their points of exit from the cord were similarly affected. Throughout the endothelial coat of the blood-vessels was unaffected and none of the vessels appeared to be thrombosed.

The *cell changes* were almost entirely confined to the anterior horns, and were extremely marked in both the cervical and lumbar enlargements. A section taken at the level of the fourth cervical segment showed about a sixth of the anterior horn cells to be normal; a few cells were shrunken and deeply-staining, but there was no evidence of any cell having completely disappeared. The rest of the cells were in various stages of tigrolysis, they were swollen, stained homogeneously a faint blue colour (Nissl method), no tigroid bodies being visible; in most of the cells the nucleus was eccentric.

At the level of the seventh cervical segment the antero-lateral group was the one most markedly affected, only a few dark-staining, shrunken remnants remaining; in the other groups of cells a little acute change was present, but in the main they were normal. At the level of the first dorsal segment much atrophy of cells was apparent. In one section not a single cell was left in the entire anterior horn, and in most only a few ragged, broken remnants could be found to represent the horn-cells. In the second dorsal segment most of the anterior horn-cells were atrophic, but a few which had survived showed tigrolysis.

In the lumbar region there was no evidence of any cells having disappeared, and none were seen in an atrophic condition. Nearly every cell was much swollen, with excentration of the nucleus and marked tigrolysis; a few cells—not more than a tenth of the entire number—were apparently normal.

It was thus clear that as a whole two kinds of cell change were present. In the first place, some of the cells had atrophied as a result of a long-standing process, whilst others were in a state of tigrolysis as a result of the morbid process which was the immediate cause of the patient's death.

The results of pathological investigation thus largely bear out what had previously been surmised. There can be little doubt that this patient succumbed to the third attack of a toxæmia which caused degeneration of the lower neurones. I would again emphasise the remarkable similarity between the terminal attack and the clinical condition seen in Landry's paralysis. If this patient had come into hospital for the first time during the final acute attack, and had shown no signs of previous nervous disease, there can be no doubt that a diagnosis of Landry's paralysis would have been made without hesitation. Whatever the pathological relationship between the two sets of conditions may be, it would seem that clinically one would have been justified in regarding this case as one of relapsing Landry's paralysis. The condition of the kidneys in this case may have been a factor predisposing to the disease by deficient elimination of toxins, but seeing that the amount of urine passed was never below the normal, I do not think they played any essential part in the production of the disease.

I am deeply indebted to Dr. Farquhar Buzzard for his care in the preparation of the specimens, and to Dr. J. S. Collier for his assistance in describing the pathological changes.

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ON CERTAIN BLOOD CHANGES IN IDIOPATHIC EPILEPSY.

BY ROBERT PUGH, M.D.EDIN.

Assistant Medical Officer, London County Asylum, Claybury.

THE following research was suggested to the writer by Dr. F. W. Mott, and the work has been carried out in the laboratory of the London County Council, Claybury; the clinical material was obtained from Claybury Asylum. The writer desires to express his deep indebtedness to Dr. Mott for having suggested the investigation, for the use of the Claybury laboratory and for numerous practical hints; to Dr. J. S. Bolton for his assistance and suggestions, and to Dr. Robert Jones for permission to use the clinical material in the Asylum, and for the facilities which he afforded him to obtain it.

In all, forty cases have been investigated, and in twenty of these a differential count of the leucocytes has been made. In all the cases the alkalinity of the blood has been estimated, and in some of the cases the effect of different drugs on the alkalinity has been determined.

The paper commences with a historical account of the previous work which has been done on the subject, and this is followed by a description of the method which has been used during the present research; an account of the cases which have been used and the results which have been obtained are then introduced; and the paper concludes with a short summary of the results of the investigation.

THE ALKALINITY.

Under normal conditions the reaction of human blood is alkaline. The alkalinity is due to the presence of two salts, *e.g.*, bicarbonate of soda $NaHCO_3$ and disodic phosphate

Na_2HPO_4. These two salts are acid salts, and are readily dissociated when brought in contact with an indicator such as litmus, forming a coloured salt. Phenolphthalein when used as an indicator gives a neutral reaction owing to the fact that it does not possess the power of dissociating these acid salts, and for this reason it cannot be employed. Thus the blood is an alkaline fluid in virtue of these two salts, which are bases in combination with very weak acids.

HISTORICAL.

Up to the present time various investigations have been carried out, and different methods used to estimate the alkalinity of the blood. The earlier investigators used the titration method. Luntz (1) titrated with phosphoric acid; Lassar (2) titrated with oxalic acid. The same objections apply to both these methods—the amount of blood required is too large, and the solution of these organic acids becomes weaker when exposed to light and air. Leibrich (3) used slabs of plaster of Paris impregnated with litmus—a drop of blood was applied' to the slab—the blood corpuscles were retained on the surface. The plasma soaked in and reacted with the absorbed litmus. Schäfer used sheets of glazed paper impregnated with litmus.

These methods were improved upon by Landois (4) in 1884. As this method has been in extensive use it may be briefly described. Blood is mixed with a solution of sulphate of soda and titrated with tartaric acid, the neutral point being estimated with litmus paper. The principle of the method consists in the prevention of coagulation by the saline solution, while the alkalinity is neutralised by the titration with tartaric acid, thus $\frac{7.5}{100}$ solution of tartaric acid is added in graduated amounts to the sulphate of soda solution. Solution 1 will contain $\frac{100 \text{ acid}}{10 \text{ sulphate}}$, solution 2 $\frac{20 \text{ acid}}{90 \text{ sulphate}}$, and so on to solution 10 $\frac{10 \text{ acid}}{100 \text{ sulphate}}$. Equal quantities of blood and one of these solutions are taken up in a pipette, and thoroughly mixed in a watch-glass, and the reaction tested with litmus paper. If the mixture is alkaline, then the next strongest acid solution is taken, and so on until the neutral point is obtained.

Drouin improved this method by titrating with oxalic acid. Again the objection is that too much blood is required, also the presence of the red blood corpuscles necessitates dilution with the saline solution, thus increasing the difficulty of accurately estimating the neutral point. In this method the alkalinity of the blood plasma and corpuscles is estimated, and in order to do this efficiently, titration must be carried out slowly and at the body temperature, so that all the corpuscles are broken down.

Haycraft and Williamson's method (5) consists of a series of glazed litmus paper treated with different strengths of sulphuric acid. This gives a series of papers of graduated acidity. A drop of blood is brought in contact with a paper of a certain strength for ten seconds, then dipped in water, and the reaction noted. The method is a simple one, but the results are not accurate enough.

Wright's method (6), which is used in this investigation and described in full. Wright claims many advantages—the quantity of blood required is small, the red blood corpuscles are completely separated from the serum, the alkalinity can be tested in a few hours, and from a clinical point of view the alkalinity of the serum is the more important because it comes into such close contact with the tissues, and may be taken as an index to the changes taking place in the circulating blood.

PHYSIOLOGY.

The alkalinity undergoes a diurnal variation, being lowest in the morning, gradually rising in the afternoon, and becoming less again in the evening (7). It is increased during digestion, owing to the passage of bicarbonate of soda from the stomach to the blood. It is decreased after severe muscular exertion, probably owing to the entrance of the products of muscular metabolism, *e.g.*, sarcolactic and carbonic acids, into the blood. Apart from these two conditions, the alkalinity is maintained at a constant level, varies within physiological limits, and may be taken as an index of the amount and activity of oxidation within the tissues.

PATHOLOGY.

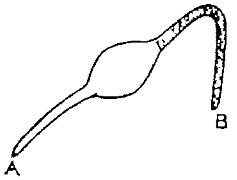
Numerous observations are recorded, noting the changes in the alkalinity in disease. These changes are constant, and manifest themselves in a diminution of the alkalinity, in diseases of the blood, *e.g.*, leucocythæmia and pernicious anæmia; in febrile and cachetic conditions; in diabetes; and especially in diabetic coma, cholera, jaundice, gout, and rheumatism. Also in certain mental diseases, *e.g.*, dementia paralytica, and epilepsy.

Charon and Biche (8), working with Landois' method, found a diminution in epilepsy, and came to the conclusion "that the epileptic attacks present nearly constant variations and in inverse relationship to the variations in the alkalinity of the blood."

Lui (9), a year later, confirmed the diminution in the alkalinity.

WRIGHT'S METHOD.

The thumb is cleansed with soap and water and sterilised with 5 per cent. solution of formalin—a solution of carbolic acid is inadmissible, as it interferes with the alkalinity of the blood. An incision is then made with a lancet, and a copious supply of blood is obtained; it is unnecessary to apply pressure to the thumb. The blood is collected in capillary tubes by means of gravity and capillary attraction, or if necessary by suction at the other end of the tube.



B is then sealed up in the blowpipe flame, the tube inverted, then A is sealed. It may be left suspended for twenty-four hours, during which the clear plasma will gravitate to the A end, the corpuscles being retained at the B end. The method used by the writer was to suspend the tube for some hours, and then to centrifuge.

Preparation of Acid Solutions and Indicator for the Analyses.

A solution of sulphuric acid is accurately standardised by precipitating with barium chloride and weighing the barium sulphate thus produced. The mother solution used is of the following value: 1 cc. = ·04155 grammes of H_2SO_4 (mean of six analyses). Dilutions of various strengths are made from this acid by running the calculated amount for the strength from the burette into a graduated cylinder and adding the requisite amount of distilled water. The dilutions first used were 10, 20, 30, 40, 60. These were supplemented by other dilutions as these became necessary during the progress of the investigation.

10-fold	dilution	1,000	cc. =	4·155	grammes	of H_2SO_4.
20	,,	,,	,,	2 0755	,,	,,
23	,,	,,	,,	1·806	,,	,,
24	,,	,,	,,	1·731	,,	,,
25	,,	,,	,,	1·662	,,	,,
26	,,	,,	,,	1·59	,,	,,
27	,,	,,	,,	1·538	,,	,,
28	,,	,,	,,	1·48	,,	,,
29	,,	,,	,,	1·43	,,	,,
30	,,	,,	,,	1·385	,,	,,
33	,,	,,	,,	1 26	,,	,,
35	,,	,,	,,	1·18	,,	,,
37	,,	,,	,,	1·12	,,	,,
40	,,	,,	,,	1·0387	,,	,,
50	,,	,,	,,	·831	,,	,,
60	,,	,,	,,	·6925	,,	,,
70	,,	,,	,,	·5935	,,	,,

The indicator used was the No. 6 special litmus paper of Grübler. This was treated according to Wright with an extremely dilute acid solution (1 in 20,000 of hydrochloric acid), washed with distilled water, and dried at 100° C.

Titration of Serum against the Standard Acid Solutions.

A capillary pipette is inserted into the serum, and the latter is allowed to flow into the tube for a distance of 2 cm. The serum is allowed to run up the pipette for a short distance in order to introduce an air bubble, and then a mark is made with a blue pencil. The end of the pipette is now quickly inserted into a solution of acid of a known strength, say the 30-fold dilution, and the acid solution is allowed to run in until the lower end of the serum column runs up to the blue mark. In this way an equal quantity of serum and of an acid of known strength is obtained. The contents of the pipette are blown out on to a clean watch glass and thoroughly mixed with the end of the pipette, aspirated, blown out again, and so on until mixing is complete. Finally the mixture is once more taken into the pipette, and a drop or two are blown on to a piece of the prepared litmus paper. The reaction is noted, and if the neutral point has not been accurately estimated fresh titrations are carried out with acids of greater or less strength until the desired reaction is obtained. Great care must be taken to standardise the acid in the first instance. Wright's results are given as dilutions of the chemically normal H_2SO_4 acid, but the acid employed in this investigation was of different strength, thus:—

1,000 cc. = 4·155 grammes of H_2SO_4
1,000 cc. = 4·9 grammes of H_2SO_4 (Wright's).

The alkalinity has been returned as the amount of H_2SO_4 in 1,000 cc. of the acid solution employed, which would exactly neutralise 1,000 cc. of serum. Thus, by alkalinity 1·385 is meant that 1,000 cc. of a solution containing this amount of H_2SO_4 would exactly neutralise the alkaline properties of 1,000 cc. of the serum.

For obtaining the normal alkalinity control cases have been selected from the staff of Claybury Asylum—physicians, clerks, porters, and attendants. Care was taken to avoid the time during which the alkalinity is said to vary, *e.g.*, after food and after severe muscular exercise. Blood was taken at a stated time, 11 a.m., on successive days from each case.

The average obtained was 1,662; one case, W. H. F., showed the highest, 1,806; this was obtained on three occasions. In all twenty cases were examined. The control cases were not taken from one class in order to show the constancy of the alkalinity, for in spite of the different conditions of living, such as diet, habits, &c., between the cases, the alkalinity was maintained at a constant value, and varied within physiological limits.

In the case of the epileptics, blood was taken from each patient at 11 a.m. on successive days during the inter-paroxsymal period, *i.e.*, an interval of seven days between seizures. The alkalinity varied; two cases showed a normal alkalinity. The average of the forty cases was below that of the control cases.

LEUCOCYTES.

The blood was obtained from the ear in nearly all the cases, and from the thumb in the remainder. The instrument used for the leucocyte count was the ordinary Thoma-Zeiss apparatus; the diluting fluid was the ordinary normal saline solution coloured with methyl violet. In all the cases 256 squares were counted, the co-efficient of error being 2 per cent. Cover glass preparations were taken at the same time, put in the incubator for an hour, held over osmic acid vapour for five minutes, replaced in the incubator for twenty-four hours, then stained with well-diluted Delafield's hæmatoxylin for five minutes, counterstained with eosin for thirty seconds, washed in methylated spirit, absolute alcohol, cleared in xylol, and mounted. In the differential count from 800 to 1,000 leucocytes were counted; four cover glass preparations were used. The nomenclature adopted in the classification of the leucocytes is taken from Clifford Allbutt's "System of Medicine."

(I.) The finely granular oxyphil polymorphonuclear contains numbers of fine granules—nucleus irregular and multipartite, phagocytic, 75 per cent.

(II.) The coarsely granular oxyphil or eosinophile contains large granules—nucleus, horseshoe, or vermiform, not phagocytic, 2 per cent.

(III.) Small hyaline or lymphocyte—nucleus large, protoplasm hyaline, no granules, 20 per cent.

(IV.) Large hyaline, larger amount of protoplasm than the small, 10 per cent.

The total number of leucocytes per cubic millimetre of blood is extremely variable—variations occur in normal individuals at different times—the normal range lies between 6,000 and 10,000. Any number below 6,000 constitutes a hypo-leucocytosis, and above 10,000 a leucocytosis. Physiological leucocytosis occurs in the new-born, in pregnancy, and during digestion. As all the cases are males and adults, the first two are excluded. In taking the leucocyte count in the interparoxysmal period, due attention was paid to the last point, and the time chosen was half an hour before meals, digestion leucocytosis thus being ruled out.

HISTORICAL.

Rutherford Macphail (11) was the first observer to note the changes in the blood in mental diseases. He states that in epilepsy the vitality is lowered and the blood is more deteriorated in male than in female patients. Of 100 cases on admission 37 per cent. recorded a lower percentage of red blood corpuscles and 40 per cent. showed a higher percentage than normal; the leucocytes varied within physiological limits. Kroumbmiller (12) who studied the blood in various psychoses, which included twelve cases of epilepsy, states that at the time of the attack the total quantity of leucocytes increases, and that this increase diminishes with every new attack; the leucocytosis is at its highest an hour after the attack. The increase is due to a relative and absolute increase of lymphocytes with a relative decrease of the older cells. He also states that a few hours after the paroxysm the coarsely granular oxyphil cells are increased.

Case 1.—Aged 16, admitted May 31, 1900; duration of epilepsy five years, bodily condition good.

Family history.—Father and mother alive, intemperate. Paternal aunt insane, patient the only child.

Mental condition.—Very dull and feeble-minded, is unable to add simple numbers, slow in answering questions. After fits is very impulsive and restless. Often has to be held down.

History of fits.—First fit five years ago, when at school. Fits gradually increased in frequency, grand mal; after an attack remains in a state of mental confusion for some hours (five to fourteen).

Record of fits from admission to December 31, 1901.—Day fits 110; night fits 207.

Alkalinity of blood during the interval 1·48.

September 24, 1901.—Seven fits from 8 p.m. to 9 50 p.m. Blood 10 p.m. alkalinity 1·0387. Blood 10.30 p m. alkalinity 1·26. Blood 11 p.m. alkalinity 1·385. Blood 12 p.m. alkalinity 1·385. Blood 1 a.m. alkalinity 1·43.

The next morning patient was very confused. Blood 10.30 a.m. alkalinity 1·43.

December 20, 1901.—Five fits from 7 a.m. to 7.45 a.m. Blood 9 a m. alkalinity 1·18. Blood 11 a.m. alkalinity 1·43. Blood 12 a.m. alkalinity 1·48. Blood 3 p.m. alkalinity 1 48.

December 25, 1901.—Five fits from 10 a.m. to 12 noon. Blood 12.30 p.m. alkalinity ·831. Blood 1 30 p.m. alkalinity 1·12. Blood 2.30 p.m. alkalinity 1·385. Blood 5.30 p.m. alkalinity 1 43.

The patient was very confused, would not answer questions, and was very irritable when spoken to.

This mental confusion lasted for eight days, and during this period blood was taken at a stated time—11 a.m. every morning. December 26, alkalinity 1·48, December 27, alkalinity 1·48, December 28, alkalinity 1·48, December 29, alkalinity 1·538; December 30, alkalinity 1 48; December 31, alkalinity 1·59; January 1, alkalinity 1·59; January 2, alkalinity 1·59.

On January 3 he was bright and cheerful, answered questions readily and expressed a desire to get up. From December 20 to January 3, he was not treated for his epilepsy.

January 5.—Was put on potas. bromid. gr. 20, three times a day. This treatment was continued until January 13. During this treatment he had three day fits, and the alkalinity was maintained at 1·538.

January 12, 1902.—About sixty seconds after his blood had been taken, he had a slight fit. Immediately prior to the fit, alkalinity 1·26; half an hour after, alkalinity 1·18; one hour after, alkalinity 1·385; two hours after, alkalinity 1·43; four hours after, alkalinity 1·538.

January 13, 1902.—Was put on suprarenal extract, one capsule three times a day after meals; on the 15th the dose was increased to six per diem. On the 20th reduced to three a day, and continued until January 29. Whilst under this treatment he had thirty-three day fits and seventeen night fits, which is a distinct increase; the mental confusion, however, was not so great, and he recovered from the after-effects of the paroxysms much sooner than when under the bromide treatment. During the intervals, there were no distinct changes in the blood; the leucocytes appeared normal, the alkalinity was not affected, the pulse was diminished in frequency by eight beats, and the blood pressure was increased.

January 30.—He was given strontii bromid. gr. 15, sodii bicarb. gr. 15, aq. ad ℥j, ℥j three times a day. This treatment was continued for two months. During this time he had four day fits and seventeen night fits, which is a pronounced decrease, the average number of fits per month being six day fits, ten night fits The alkalinity was maintained at a fairly constant value, and varied from 1·48 to 1·662.

Leucocytes. — Interparoxysmal period, 9,500. Differential count:—Polymorphonuclear, 65 per cent.; large hyaline, 6 per cent.; small hyaline, 25 per cent.; eosinophile, 3 per cent. Ten minutes after seven fits:—Leucocytes, 10,000. Differential count:—Polymorphonuclear, 68 per cent.; large hyaline, 8 per cent.; small hyaline, 23 per cent.; eosinophile, 4 per cent. Sixty minutes later:—Leucocytes, 21,000. Differential count:—Polymorphonuclear, 60 per cent.; eosinophile, 5 per cent.

Case 2.—Aged 18. Admitted August 7, 1900. Duration of epilepsy, nine years; bodily condition good.

Family history.—Father died of acute Bright's disease aged 36, an alcoholic. Mother alive and well; six children, four boys, two girls; patient is the fifth child; the sixth child is also an epileptic.

Mental condition.—Is rational in manner and talk, slight impairment of memory; is very intractable after fits.

History of fits.—Developed his epilepsy at nine years of age, his mother states that he had a fall on his head when six years of age. Grand mal. Recovery from mental confusion gradual, two minutes before a fit the right lower eyelid twitches.

Record of fits from admission to December 31, 1901.—Day fits, 44; night fits, 81.

Alkalinity in the interparoxysmal period, 1·538. Slight fit 8 a.m. Blood 11 a.m. alkalinity 1·385. Blood 2.30 p.m. alkalinity 1·538.

Two fits 9.30 p.m. Blood 10.30 p.m. alkalinity 1.26. Blood 11.30 p.m. alkalinity 1·385. Blood 1 a.m. alkalinity 1·48.

Blood 7.30 p.m. alkalinity 1·59. Blood 11 a.m. alkalinity 1·43. Blood 12 noon alkalinity 1·48. Blood 3 p.m. alkalinity 1.48.

January 12, 1902.—About sixty seconds after his blood had been taken he had a slight fit.

Immediately prior to the fit, alkalinity 1·26; half an hour after, alkalinity 1·18; one hour after, alkalinity 1·385; two hours after, alkalinity 1·43; four hours after, alkalinity 1·538.

Leucocytes.—The study of the blood ten minutes after the fit shows leucocytes 9,500. An hour after:—There is a distinct leucocytosis 14,000. Differential count:—Polymorphonuclear, 60 per cent.; small hyaline, 25 per cent.; large hyaline, 11 per cent.; eosinophile, 4 per cent.

Case 3.—Aged 18. Admitted August 24, 1900. Duration of epilepsy, fourteen years. Bodily condition fair, stature short, suffers from constipation.

Family history.—Father and mother (Jews) dead, both intemperate; patient the only son; one sister alive and healthy. Maternal uncle insane, committed suicide.

Mental condition.—Is simple and childish in manner and talk, is easily confused, mental reaction slow. Answers questions slowly. Memory for recent events impaired.

History of fits.—Said to be healthy and intelligent up to 1886, when his father died suddenly. Soon after this patient had two epileptic fits. Grand mal. Mental confusion lasts about one and a half hours.

Record of fits from admission to December 31, 1901.—Day fits, 275 , night fits, 450.

Alkalinity in the interparoxysmal period, 1·48.

December 2.—Eight fits from 10.30 a.m. to 11 a.m.

Blood 11.15 a.m. alkalinity ·831. Blood 12 noon alkalinity 1·26. Blood 1 p.m. alkalinity 1·385. Blood 3 p m. alkalinity 1·48.

At 4 p.m. patient was very restless and irritable, and a little confused. At 7.30 he had ten very severe fits, and was given an enema of potas. brom. gr. 30, chloral hydrate. gr. 15.

Blood 7.45 p.m. alkalinity 1·18. Blood 8.30 p.m. alkalinity 1·385. Blood 9.30 p.m. alkalinity 1·26. Blood 11.30 p.m. alkalinity 1 48.

During the month of December the potassium bromide was suspended, and he had 97 day fits and 41 night fits.

December 15.—Fifteen fits 11.50 p.m. to 12.30 a.m.

Blood 12.40 a.m. alkalinity ·831. Blood 1 a.m. alkalinity 1·26. Blood 10.30 a.m. alkalinity 1·538.

December 21.—Fourteen fits 8.30 p.m. to 9 p.m.

Blood 9.15 p.m. alkalinity 1·0387. Blood 10 p.m. alkalinity 1·385. Blood 11 p.m. alkalinity 1·43. Blood 12 midnight alkalinity 1·48.

January 13, 1902.—Was put on suprarenal extract, one capsule three times a day after meals. On the 17th the dose was increased to six per diem ; on the 22nd the dose was reduced to three per diem. This treatment was continued until February 1. The effects produced were essentially similar to those produced in Case 1. The fits increased in frequency; the record for the eighteen days reads:—11 day fits, 154 night fits. The marked increase of the nocturnal fits is very striking, and is five-fold greater than the average monthly record. The nearest approach to these figures was in June, 1901, when the patient had 121 night fits

Blood—No distinct change in the alkalinity, which varied from 1·48 to 1·538. The leucocytes appeared normal.

Pulse.—Diminished in frequency by nine beats on an average, and the blood pressure was increased. January 14, 11 a.m., 125 mm. January 16, 11 a.m., 130 mm. January 18, 11 a.m., 130 mm. January 21, 11 a.m., 145 mm. January 26, 11 a.m., 145 mm.

The effect upon the mental state was good, and the recovery from the confusion following the fit was rapid.

January 30, 1902.—He was put on strontii bromidi gr. 15, sodii bicarb. gr. 15, aq. ad ℥j, ℥j, three times a day.

February 12.—The mixture was given four times a day for twelve days, and from February 24 to the end of March three times a day. Under this treatment the number of fits was considerably decreased, and during the month of February the patient did not have a fit. The alkalinity was maintained at a constant value, *e.g.*, 1·538 to 1·662.

Leucocytes.—Interparoxysmal period, 9,200. Differential count:—Polymorphonuclear, 68 per cent.; large hyaline, 7 per cent.; small hyaline, 22 per cent.; eosinophile, 3 per cent. Forty minutes after eight fits:—Leucocytes, 19,000. Differential count:—Polymorphonuclear, 60 per cent.; large hyaline, 8 per cent.; small hyaline, 30 per cent.; eosinophile, 2 per cent.

Case 4.—Aged 19, admitted May 15, 1900. Duration of epilepsy, seven years. Bodily condition good.

Family history.—Father and mother alive and well. Insanity and phthisis on mother's side. Patient the only child alive; his brother died of phthisis, aged 18.

Mental condition.—Is rational in manner and talk in the intervals. Memory slightly impaired. Is very fanciful and restless after fits, and develops delusions of persecution.

History of Fits.—Developed epilepsy at 12 years of age; the fits gradually increased in frequency; the month before admission he had over 100 fits. Grand mal, mostly nocturnal; recovery from mental confusion rapid.

Record of fits from admission to December 31, 1901.—Day fits, 693; night fits, 830.

Alkalinity in the interparoxysmal period, 1·43; three hours after his blood had been taken the patient had a strong fit—3 p.m. Blood 3.15 p.m. alkalinity 1·0387. Blood 4 p.m. alkalinity 1·26. Blood 5 p.m. alkalinity 1·43. Blood 8 p.m. alkalinity 1·538.

January 13, 1902.—Was put on suprarenal extract, one capsule three times a day. On the 17th the dose was increased to six a day. This treatment was carried out for eighteen days. The fits increased in frequency, but not to such an extent as in Cases 1 and 3. There were no distinct changes in the blood, the leucocytes were normal, but the alkalinity varied; on two occasions it was 1·43.

Pulse.—Diminished in frequency by six beats, the blood pressure was increased. The effect upon the mental state was very pronounced, the after-effects passing off in a short time.

Leucocytes.—Interparoxysmal period, 10,000. Differential count:—Polymorphonuclear, 70 per cent.; large hyaline, 6 per cent.; small hyaline, 21 per cent.; eosinophile, 3 per cent. Four hours after a fit:—Leucocytes, 12,000 Differential count:—Polymorphonuclear, 62 per cent.; large hyaline, 4 per cent.; small hyaline, 30 per cent.; eosinophile, 5 per cent.

Case 5.—Aged 33, admitted October 18, 1893. Duration of epilepsy unknown. Bodily condition fair.

No family history obtained.

Mental condition.—Is dull, lost, and feeble-minded. After fits is restless, and has hallucinations of sight.

History of fits.—Grand mal. Epigastric aura. Mental confusion lasts about three hours.

Record of fits from admission to December 31, 1901.—Day fits, 305 night fits, 448.

Interparoxysmal alkalinity, 1·662, 1·538. Five fits in quick succession. Blood fifteen minutes after, alkalinity ·831. Blood one hour after, alkalinity 1·26. Blood two hours after, alkalinity 1·385. Blood four hours after, alkalinity 1·48. Blood twelve hours after, alkalinity 1·662. Alkalinity during aura, 1·26.

Leucocytes.—Twelve hours after five fits:—Leucocytes, 11,000. Differential count:—Polymorphonuclear, 70 per cent.; large hyaline, 7 per cent.; small hyaline, 18 per cent.; eosinophile, 5 per cent.

Case 6.—Aged 46, admitted September 10, 1896. Duration of epilepsy three years. Bodily condition fair.

Family History.—Father and mother dead. Paternal uncle insane. Patient the only child.

Mental condition.—Is demented; has very little idea of time or place; after fits is very restless and irritable, and develops religious delusions.

History of fits.—Had his first fit three years ago after a drinking bout. Grand mal. Mental confusion lasts about three hours.

Record of fits from admission to December 31, 1901.—Day fits, 81; night fits, 114.

Interparoxysmal alkalinity, 1·662 to 1·538. Two strong fits. Blood 20 minutes after, alkalinity 1·0387. Blood half an hour after, alkalinity 1·12. Blood one hour after, alkalinity 1·26. Blood two hours after, alkalinity 1·43. Blood five hours after, alkalinity 1·538.

Sixty minutes after:—Leucocytes 18,000. Differential count:—Polymorphonuclear, 58 per cent.; large hyaline, 8 per cent.; small hyaline, 33 per cent.; eosinophile, 2 per cent

Case 7.—Aged 40, admitted May 25, 1895. Duration of epilepsy, ten years; bodily condition good.

Family history.—Father died of pneumonia, an alcoholic; mother alive and healthy; two brothers alive and well.

Mental condition.—Very rambling and incoherent in talk. Memory much impaired especially for recent events; expresses "electrical" delusions.

History of fits.—Had his first fit when 30 years of age, at which time he was travelling with a circus; no history of drink. Grand mal; mental confusion lasts about three hours.

Record of fits from admission to December 31, 1901.—Day fits, 332; night fits, 328.

Interparoxysmal alkalinity, 1·538. Slight fit 10.40 a.m. Blood 11·5 a.m. alkalinity 1·18. Blood 11·45 a.m. alkalinity 1·26. Slight fit 12 10 p.m. Blood 12.30 p.m. alkalinity 1·0387. Blood 1 30 p.m. alkalinity 1·26. Blood 3.30 p.m. alkalinity 1·43. Blood 5.30 p.m. alkalinity 1·538.

Fifty minutes after the second fit:—Leucocytes 19,000.

Differential count:—Polymorphonuclear, 59 per cent.; large hyaline, 30 per cent.; small hyaline, 30 per cent.; eosinophile, 3 per cent.

Case 8.—Aged 19, admitted August 8, 1900. Duration of epilepsy, three years. Bodily condition good.

Family history.—Father died of heart disease, intemperate. Mother alive and healthy. Maternal uncle died of phthisis. Patient was the only child.

Mental condition.—Is very unstable, restless, and irritable, and is given to introspection; after fits is pugnacious, intractable and suicidal.

History of fits.—Had his first fit when 16 years old, then had a fit every week for six weeks, and then ceased having them for eight weeks. The fits gradually increased in frequency and severity. Grand mal. Recovers quickly from the mental confusion.

Record of fits from admission to December 31, 1901.—Day fits, 94; night fits, 236.

Interparoxysmal alkalinity 1·538.—Fit 11.30 a.m. Blood 11.40 a.m. alkalinity 1·12. Blood 12.30 p.m. alkalinity 1·385. Blood 1.30 p.m. alkalinity 1·48. Blood 3.30 p.m. alkalinity 1 538.

Forty minutes after two fits:—Leucocytes, 17,000. Differential count:—Polymorphonuclear, 60 per cent.; large hyaline, 29 per cent.; small hyaline, 10 per cent.; eosinophile, 1 per cent.

Case 9.—Aged 25, admitted December 28, 1900. Duration of epilepsy, fifteen years. Bodily condition good.

Family history.—Father and mother alive and healthy, both intemperate. Two brothers alive and healthy. Patient the third child. One sister simple-minded.

Mental condition.—After fits is very impulsive, religious and emotional. Slight mental impairment.

History of fits.—Developed his epilepsy at 10 years of age. The fits gradually increased in frequency. Grand mal. Laryngeal aura. Recovery from mental confusion gradual (in about three hours).

Interparoxysmal alkalinity 1·538; forty seconds before fit 1·26; half an hour after, alkalinity 1·18; one hour after, alkalinity 1·385; two hours after, alkalinity 1·43; six hours after, alkalinity 1·538.

Eighty minutes after one fit:—Leucocytes, 12,400. Differential count:—Polymorphonuclear, 68 per cent.; large hyaline, 23 per cent.; small hyaline, 6 per cent.; eosinophile, 3 per cent.

Case 10.—Aged 31, admitted October 24, 1896. Duration of epilepsy, five years. Bodily condition good.

No family history obtained.

Mental condition.—Is dull, stupid, and feeble-minded. Memory very defective, has no idea of time. After fits is irritable, and develops persecutory delusions.

History of fits.—Grand mal. Mental confusion lasts about three hours.

Record of fits from admission to December 31, 1901.—Day fits, 954; night fits, 527.

Interparoxysmal alkalinity, 1·48. Fit 8 a.m. Blood 11 a.m. alkalinity 1·385. Blood 2.30 p.m. alkalinity 1·538. Strong fit 2.45 p.m. Blood 3.30 p.m. alkalinity 1·12. Blood 4.45 p.m. alkalinity 1·385. Blood 8 p.m. alkalinity 1·538. Two fits 9 p.m. Blood 9.15 p.m. alkalinity ·831. Blood 10 p.m. alkalinity 1·12. Blood 11 p.m. alkalinity 1·26. Blood 1 a.m. alkalinity 1·48.

Fifty minutes after the fit:—Leucocytes, 14,000. Differential count:—Polymorphonuclear, 60 per cent.; eosinophile, 3 per cent.; large hyaline, 8 per cent.; small hyaline, 30 per cent.

Case 11.—Aged 21, admitted February 2, 1900. Duration of epilepsy, eight years. Bodily condition fair; suffers from constipation and indigestion.

Family history.—Father alive and well. Mother died of cancer, aged 44. Epilepsy and phthisis on mother's side.

Mental condition.—Is simple in manner and talk; slight mental impairment. After fits is restless and irritable, and develops persecutory delusions.

History of fits.—Had his first fit when 13 years of age. Grand mal. Epigastric aura five minutes before the fit. Recovery from mental confusion gradual

Record of fits from admission to December 31, 1901.—Day fits, 156; night fits, 107.

Interparoxysmal alkalinity, 1·48. Alkalinity during aura 1·385. Half an hour after fit, 1·18; one hour after fit, 1·385; two hours after fit, 1·48; four hours after fit, 1·538.

Twelve hours after one fit:—Leucocytes, 9,000. Differential count:—Polymorphonuclear, 70 per cent; large hyaline, 7 per cent.; small hyaline, 20 per cent.; eosinophile, 3 per cent.

Case 12.—Aged 46, admitted August 24, 1893. Duration of epilepsy, twenty years. Bodily condition good.

No family history obtained.

Mental condition.—Is very restless and irritable, and talks much and foolishly on religious subjects. Is very demented; has no idea of time or place.

History of fits.—Has very frequent petit mal seizures. Mental confusion lasts about an hour.

Record of fits from admission to December 31, 1901.—Day fits, 170; night fits, 27.

Alkalinity in the paroxysmal period, 1·538. Alkalinity twenty seconds before a fit, 1·385. Fit 11 a.m. Blood 11.15 a.m. alkalinity 1·385. Blood 12.15 p.m. alkalinity 1·48. Blood 2 p.m. alkalinity 1·538. Three strong fits 7 p.m. Blood 7.20 p.m. alkalinity ·831. Blood 8 p.m. alkalinity 1·12. Blood 9 p.m. alkalinity 1·26. Blood 11 p.m. alkalinity 1·43. Blood 1 a.m. alkalinity 1·48.

One hour after three fits:—Leucocytes, 23,000. Differential count:—Polymorphonuclear, 58 per cent.; large hyaline, 8 per cent.; small hyaline, 32 per cent.; eosinophile, 3 per cent.

Case 13.—Aged 49, admitted November 22, 1897. Duration of epilepsy, 43 years. Bodily condition fair, suffers from constipation and gastric catarrh.

Family history.—Father died in an epileptic fit. Mother alive, intemperate; maternal aunt insane.

Mental condition.—Is dull, stupid, and very demented. After fits is restless, irritable, and impulsive.

History of fits.—Had his first fit when six years of age. He did not have a second until fifteen years later. This was followed by another four years afterwards, then they became more frequent. Grand mal, no aura. Mental confusion lasts about four hours.

Record of fits from admission to December 31, 1901:—Day fits, 32; night fits, 117.

Interparoxysmal alkalinity, 1·538 : 1·48. Two fits 8.30 p.m. Blood 9 p.m. alkalinity 1·12. Blood 10 p.m. alkalinity 1·26. Blood 12 midnight alkalinity 1·43. Blood 1 a.m. alkalinity 1·48.

One and a half hours after one fit:—Leucocytes, 20,000. Differential count:—Polymorphonuclear, 58 per cent.; large hyaline, 6 per cent.; small hyaline, 39 per cent.; eosinophile, 2 per cent.

Case 14.—Aged 22. Admitted August 22, 1896. Duration of epilepsy, ten years. Bodily condition fair.

Family history.—Father and mother alive and healthy. One brother alive and well.

Mental condition.—Is dull, slow, and feeble-minded. Memory for recent events defective. After fits is dazed, destructive, and impulsive.

History of fits.—Developed his epilepsy when twelve years of age. Grand mal. Has a severe frontal headache half an hour before the fit. Mental confusion lasts about four and a half hours.

Record of fits from admission to December 31, 1901 :—Day fits, 445; night fits, 834.

Interparoxysmal alkalinity, 1·538 : 1·48. Four fits from 10 a.m to 11 a.m. Blood 11.30 a.m. alkalinity 1·12. Blood 1 p.m. alkalinity 1·385. Blood 3 p.m. alkalinity 1·48. Blood 6 p.m. alkalinity 1·59. Alkalinity during aura, 1·385.

Six hours after four fits :—Leucocytes, 11,000. Differential count:—Polymorphonuclear, 61 per cent.; large hyaline, 6 per cent.; small hyaline, 25 per cent.; eosinophile, 8 per cent.

Case 15.—Aged 28. Admitted January 25, 1900. Duration of epilepsy, twenty-two years. Bodily condition good.

Family history.—Father alive, very intemperate. Mother dead, cause unknown. Maternal uncle died of paralysis.

Mental condition.—Is very feeble-minded. Memory defective, has no idea of time. After fits is irritable, and has hallucinations of sight.

History of fits.—Developed his epilepsy when six years old. Grand mal. No warning. Mental confusion lasts about three hours.

Record of fits from admission to December 31, 1901.—Day fits, 105; night fits, 172.

Interparoxysmal alkalinity, 1·538. One severe fit 8.30 p.m. Blood 9 p.m. alkalinity 1·26. Blood 10 p.m. alkalinity 1·385. Blood 11 p.m. alkalinity 1·48. Blood 1 a m. alkalinity 1·59.

Twenty-four hours after two fits :—Leucocytes, 9,000. Differential count:—Polymorphonuclear, 70 per cent.; large hyaline, 4 per cent.; small hyaline, 23 per cent.; eosinophile, 3 per cent.

Case 16.—Aged 31. Admitted December 8, 1899. Duration of epilepsy not known. Bodily condition fair, suffers from constipation.

Mental condition.—Is simple and childish in manner and talk; mental reaction slow, memory very defective.

History of fits.—Grand mal, no aura; mental confusion lasts about three hours.

Record of fits from admission to December 31, 1901.—Day fits, 16; night fits, 162.

Interparoxysmal alkalinity, 1·538 : 1·48. Three fits, ten minutes' interval between the seizures. Blood half an hour after, alkalinity 1·12. Blood one hour after, alkalinity 1·26. Blood three hours after, alkalinity 1·48. Blood five hours after, alkalinity 1·59. Blood twelve hours after, alkalinity 1·59.

Eight hours after one fit:—Leucocytes, 8,000. Differential count:—Polymorphonuclear, 62 per cent.; large hyaline, 6 per cent.; small hyaline, 23 per cent.; eosinophile, 9 per cent.

Case 17.—Aged 34, admitted August 15, 1893. Duration of epilepsy, seven years. Bodily condition fair.

No family history obtained.

Mental condition.—Is very dull and feeble-minded. Memory much impaired, has no idea of time. After fits is restless and intractable.

History of fits.—Had his first fit seven years ago. Grand mal. No warning. Mental confusion lasts three hours.

Record of fits from admission to December 31, 1901.—Day fits, 490; night fits, 998.

Interparoxysmal alkalinity, 1·59 : 1·48. Ten minutes after two fits, alkalinity 1·0387. Thirty minutes after two fits, alkalinity 1·16. Two hours after two fits, alkalinity 1·385. Three hours after two fits, alkalinity 1·48. Six hours after two fits, alkalinity 1·59.

Three days after one fit:—Leucocytes, 12,000. Differential count:—Polymorphonuclear, 56 per cent.; large hyaline, 7 per cent.; small hyaline, 32 per cent.; eosinophile, 5 per cent.

Case 18.—Aged 52, admitted September 30, 1896. Duration of epilepsy not known. Bodily condition fair.

No family history obtained.

Mental condition.—Is dull, stupid, and childish in manner and conversation. Memory much impaired. After fits has hallucinations of smell and becomes abusive.

History of fits.—Grand mal, no aura. Mental confusion lasts about three hours.

Record of fits from admission to December 31, 1901.—Day fits, 443; night fits, 313.

Interparoxysmal alkalinity, 1·538. Fit 1 p.m. Blood 2 p.m. alkalinity 1·26. Blood 3 p.m. alkalinity 1·385. Blood 5 p.m. alkalinity 1·48. Blood 7.30 p.m. alkalinity 1·59.

Three hours after two fits:—Leucocytes, 13,000. Differential count:—Polpmorphonuclear, 52 per cent.; large hyaline, 7 per cent.; small hyaline, 38 per cent.; eosinophile, 3 per cent.

Case 19.—Aged 19, admitted March 8, 1900. Duration of epilepsy, two years Bodily condition good.

No family history obtained.

Mental condition.—Is very feeble-minded and is unable to read or write. Habits very faulty. Has very little idea of time or place.

History of fits.—Has always been dull and stupid. Had his first fit two years ago, and during the following twelve months had several slight seizures. A few months before admission he had numerous strong fits. Grand mal. Recovery from mental confusion gradual.

Record of fits from admission to December 31, 1901.—Day fits, 50; night fits, 55.

Interparoxysmal alkalinity, 1·538. Fit 11 a.m. Blood 12 noon alkalinity 1·385. Blood 1 p.m. alkalinity 1·43. Blood 3 p.m. alkalinity 1·48. Blood 7 p.m. alkalinity 1·59.

Four days after one fit:—Leucocytes, 9,000. Differential count:—polymorphonuclear, 68 per cent.; large hyaline, 8 per cent.; small hyaline, 20 per cent.; eosinophile, 4 per cent.

Case 20.—Aged 22, admitted October 18, 1894. Duration of epilepsy, 4 weeks. Bodily condition good.

No family history obtained.

Mental condition.—Is emotional and intractable; memory defective. After fits is intensely noisy, violent, and impulsive, and develops persecutory delusions.

History of fits.—Had his first fit four weeks prior to admission. Grand mal, epigastric aura. Mental confusion lasts about four hours.

Record of fits from admission to December 31, 1901.—Day fits, 303; night fits, 1,845.

Interparoxysmal alkalinity, 1·538 : 1·48. Taken at 2 a.m., 1·43. Two fits in quick succession. Blood half an hour after, alkalinity 1 0387. Blood one hour after, alkalinity 1·26. Blood two hours after, alkalinity 1·43. Blood four hours after, alkalinity 1·59. Blood twenty-four hours after, alkalinity 1·59.

Four hours after two fits:—Leucocytes, 14,000. Differential count:—Polymorphonuclear, 57 per cent.; large hyaline, 5 per cent.; small hyaline, 34 per cent.; eosinophile, 5 per cent.

Case 21.—Aged 26, admitted August 11, 1899. Duration of epilepsy thirteen years. Bodily condition good.

Family history—Father and mother alive and healthy; two brothers living, healthy; one brother died abroad, cause unknown. Patient has had syphilis.

Mental condition.—Is simple and childish in manner. Does not appreciate his surroundings, is very demented, has very little idea of time.

History of fits.—Had his first fit thirteen years ago. The fits gradually increased in frequency. After fits was very restless and intractable.

Record of fits from admission to December 31, 1901.—Day fits, 172; night fits, 150.

For the last seven months all his fits have been nocturnal. Alkalinity in the interparoxysmal period 1·48. Nine hours before a fit, 1·43. Fit 9.30 p.m. Blood 9.50 p.m. alkalinity 1.12. Blood 10.50 p.m. alkalinity 1.26. Blood 11.50 p.m. alkalinity 1·385. Blood 10.30 a.m. alkalinity 1·538.

Patient was subjected to the suprarenal treatment for twenty-one days, apparently without any effect. The fits did not increase in frequency, and there was no perceptible rise in the blood pressure.

Case 22.—Aged 21, admitted March 22, 1894. Duration of epilepsy, fourteen years. Bodily condition feeble, poorly nourished. Palate high.

No family history obtained.

Mental condition.—Is very simple-minded, is of low intellect, is unable to add simple numbers, rambles incoherently. After fits is irritable, impulsive, and abusive.

History of fits.—Had his first fit when seven years of age. A short time before admission had an attack of status epilepticus. Grand mal, no aura.

Record of fits from admission to December 31, 1901.—Day fits, 531; night fits, 162.

Interparoxysmal alkalinity 1·538 : 1·48. Two slight fits 9 a.m. Blood 9.30 a.m. alkalinity 1·12. Blood 11 a.m alkalinity 1·43. Blood 1 p.m. alkalinity 1·43. Blood 5 p.m. alkalinity 1·59.

Case 23.—Aged 32, admitted November 8, 1895. Duration of epilepsy, twenty-nine years. Bodily condition fair, suffers from indigestion.

No family history obtained.

Mental condition.—Is dull and feeble-minded; mental reaction is slow; he is easily excited, and is very unstable. Memory very defective; has very little idea of time or place; after fits is violent and impulsive.

History of fits.—Had his first fit when three years of age, and then had three fits a month up to 14 years of age. He had no fits from 14 to 25, and since the latter age he has had them frequently. Grand mal. Precordial aura, which he describes as "a pleasant feeling as though his heart were stopping."

Record of fits from admission to December 31, 1901. Day fits, 475; night fits, 73.

Interparoxysmal alkalinity 1·48 : 1·43. Alkalinity during aura 1·26; alkalinity thirty minutes after fit, 1·18; alkalinity one hour after fit, 1·26; alkalinity three hours after fit, 1·43; alkalinity six hours after fit, 1·59.

Case 24.—Aged 43, admitted April 30, 1894. Duration of epilepsy, fifteen years. Bodily condition fair; muscular movements very tremulous.

Family history.—Father, mother, and one sister insane at Brookwood Asylum. Brother committed suicide.

Mental condition.—Is dull, morose, and feeble-minded; after fits is restless and wanders aimlessly round the ward; has hallucinations of sight and hearing.

History of fits.—Had his first fit when twenty-eight years of age. Grand mal, no aura. Mental confusion lasts about five hours.

Record of fits from admission to December 31, 1901.—Day fits, 46; night fits, 83.

Interparoxysmal alkalinity 1·538 : 1·48. Three fits from 9 a.m. to 11 a.m. Blood 11.30 a.m. alkalinity 1·0387. Blood 12 noon alkalinity 1·26. Blood 2 p.m. alkalinity 1·43. Blood 5 p.m. alkalinity 1·538. Blood 10 p.m. alkalinity 1·538.

Case 25.—Aged 26, admitted October 19, 1893. Duration of epilepsy, six years. Bodily condition fair.

Family history.—Father and mother alive and healthy. No history of insanity, epilepsy, or phthisis.

Mental condition.—Is simple and childish in manner, incoherent in his remarks, expresses delusions of persecution, says "people follow him about to shoot him"; after fits is violent and abusive.

History of fits.—Had his first fit six years ago. It was stated to be caused by a large piece of wood falling on his head. Grand mal; left eyelid twitches three minutes prior to the fit. Mental confusion lasts about four hours.

Record of fits from admission to December 31, 1901:—Day fits, 115; night fits, 411.

Interparoxysmal alkalinity, 1 538 : 1·43. Alkalinity during aura, 1·26. Alkalinity fifteen minutes after fit, 1·0387. Alkalinity one hour after fit, 1·385. Alkalinity two hours after fit, 1·48. Alkalinity four hours after fit, 1·538. Alkalinity twelve hours after fit, 1·59.

Case 26.—Aged 21, admitted November 1, 1894. Duration of epilepsy, not known. Bodily condition fair; usually constipated. No family history obtained.

Mental condition.—Is simple and childish in manner and talk. After fits is irritable and quarrelsome, and develops delusions of persecution.

History of fits.—Patient says he has had fits since nine years old. Grand mal; aura two minutes prior to the fit, which he describes as a painful sensation in his right forearm. Mental confusion lasts about six hours.

Record of fits from admission to December 31, 1901:—Day fits, 378; night fits, 456.

Interparoxysmal alkalinity, 1·538 : 1·48. Alkalinity sixty seconds before a fit, 1·18. Alkalinity one hour after, 1·26. Alkalinity two hours after, 1·385. Alkalinity four hours after, 1·538. Alkalinity twelve hours after, 1·59.

Case 27.—Aged 26, admitted November 3, 1893. Duration of epilepsy thirteen years. Bodily condition fair. Palate high and arched. Is myopic.

Family history.—Father died of lead palsy, intemperate. Mother alive and healthy. Maternal grandfather died of phthisis.

Mental condition.—Is simple and childish in manner and talk; mental reaction slow. Intellect weak. Memory defective. After fits is troublesome, irritable, emotional and impulsive.

History of fits.—Had his first fit when 13 years of age. Had "brain fever" when 4. Grand mal. Epigastric aura. Mental confusion lasts about four hours.

Record of fits from admission to December 31, 1901. Day fits, 420; night fits, 121.

Interparoxysmal alkalinity 1·48; half an hour after two severe fits, alkalinity 1·0387; one hour after two severe fits, alkalinity 1·26; two hours after two severe fits, alkalinity 1·385; four hours after two severe fits, alkalinity 1·538; twelve hours after two severe fits, alkalinity 1·59.

Case 28.—Aged 24, admitted January 31, 1902. Duration of epilepsy three years. Bodily condition fair.

Family history. Father and mother alive and healthy. A brother insane, died at Hanwell Asylum seven years ago. One sister insane at Salisbury Asylum.

Mental condition.—Is simple and childish in manner and talk. Memory defective; is unable to give a coherent account of himself; after fits is very excited.

History of fits.—Developed his epilepsy when 21 years of age. Grand mal, no aura. Mental confusion lasts about five hours. He has had several strong fits since admission.

Interparoxysmal alkalinity, 1·538 : 1·48. Two strong fits 10 a.m. Blood 10·30 a.m. alkalinity 1.0387. Blood 11 a.m. alkalinity 1·26. Blood 1 p.m. alkalinity 1·43. Blood 5 p.m. alkalinity 1·538. Blood 8 p.m. alkalinity 1·538.

Case 29.—Aged 27, admitted October 14, 1899. Duration of epilepsy, twenty years. Bodily condition fair. Mitral disease. Usually constipated.

No family history obtained.

Mental condition.—Is dull and feeble-minded, mental reaction slow. Memory defective for recent events. After fits is restless and impulsive.

History of fits.—Had his first fit when 7 years of age, said to follow scarlet fever. Grand mal, no aura. Mental confusion lasts about four hours.

Record of fits from admission to December 31, 1901.—Day fits, 71; night fits, 225.

Interparoxysmal alkalinity 1·48 : 1·43. Strong fit 2 p.m. Blood 2.20 p.m. alkalinity 1·12. Blood 3 p.m. alkalinity 1·26. Blood 5 p.m. alkalinity 1·48. Blood 7 p.m. alkalinity 1·538.

Case 30.—Aged 44, admitted November 4, 1893. Duration of epilepsy, six years. Bodily condition good.

Family history.—Father and mother dead. Two uncles and grandfather died of phthisis.

Mental condition.—Is dull and feeble-minded. Memory much impaired, especially for recent events. After fits is irritable, grumbles much and says his food is poisoned.

History of fits.—Developed his epilepsy when 38 years of age Grand mal, no aura. Mental confusion lasts about five hours.

Record of fits from admission to December 31, 1901.—Day fits, 188; night fits, 219.

Interparoxysmal alkalinity, 1·48. Half an hour after two fits, alkalinity 1·0387; one hour after two fits, alkalinity 1·26; two hours after two fits, alkalinity 1·43; three hours after two fits, alkalinity 1·538; five hours after two fits, alkalinity 1·538; eight hours after two fits, alkalinity 1·59.

Case 31.—Aged 19, admitted October 12, 1893. Duration of epilepsy, ten years. Bodily condition good.

No family history obtained.

Mental condition.—Is very dull and feeble-minded, restless after fits, and expresses vague delusions of persecution. Memory very defective.

History of fits.—Grand mal. Mental confusion lasts about three hours.

Record of fits from admission to December 31, 1901.—Day fits, 348; night fits, 762.

Interparoxysmal alkalinity 1·538. Five fits from 7 a.m. to 10.30 a.m. Blood 11 a m. alkalinity ·831. Blood 1 p.m. alkalinity 1·26. Blood 2 p.m. alkalinity 1·43. Blood 5 p.m. alkalinity 1·59. Blood 9.30 p.m. alkalinity 1·538.

Case 32.—Aged 44, admitted August 17, 1895. Duration of epilepsy, thirty years. Bodily condition fair; is usually constipated.

No family history obtained.

Mental condition.—Is dull and feeble-minded. Memory much impaired. After fits is troublesome, restless, and impulsive.

History of fits.—Has had fits for 30 years. Grand mal, taste aura. Mental confusion lasts about five hours.

Record of fits from admission to December 31, 1901.—Day fits, 691; night fits, 199.

Interparoxysmal alkalinity, 1·538 : 1·48. Two strong fits 9 a.m. Blood 9.30 a.m. alkalinity 1·18. Blood 11 a m. alkalinity 1·43. Blood 1 p.m. alkalinity 1·48. Blood 3 p.m. alkalinity 1 59. Blood 7 p.m. alkalinity 1·59.

Case 33.—Aged 23, admitted February 19, 1896. Duration of epilepsy, seventeen years. Bodily condition fair, suffers from indigestion.

Family history.—Father dead, cause unknown. Mother dead, cause heart disease. Patient the only child.

Mental condition.—Is simple and childish in manner and talk; has some religious exaltation with mild excitement.

History of fits.—Had his first fit when six years of age; did not have another for ten years; since that time he has had them frequently. Grand mal, no aura. Mental confusion lasts three hours.

Record of fits from admission to December 31, 1901.—Day fits, 575; night fits, 208.

Interparoxysmal alkalinity, 1·48 : 1·43. One slight fit 2 p.m

Blood 3 p.m. alkalinity 1·385. Blood 4 p.m. alkalinity 1·48. Blood 6 p.m. alkalinity 1·59. Blood 10 p.m. alkalinity 1.59.

Case 34.—Aged 40, admitted November 11, 1895. Duration of epilepsy, twenty-four years. Bodily condition fair; pupils irregular, left contracted.

No family history obtained.

Mental condition.—Is dull, confused, and simple-minded. Memory much impaired; has no idea of time; after fits is violent, hears voices, and chatters to them.

History of fits.—Had his first fit when sixteen years of age. Grand mal, no aura. Mental confusion lasts six hours.

Record of fits from admission to December 31, 1901.—Day fits, 77; night fits, 352.

Interparoxysmal alkalinity, 1·538 : 1·48. Three strong fits from 1 p m. to 2.30 p.m. Blood 2.45 p.m. alkalinity 1·0387. Blood 4.30 p.m. alkalinity 1·385. Blood 6.30 p.m. alkalinity 1·59. Blood 10.30 p.m., alkalinity 1·538.

Case 35.—Aged 65, admitted February 1, 1898. Duration of epilepsy, ten years. Bodily condition fair. Arteries very atheromatous, albumen in urine. Has been in the army, and lived twelve years in India. Scar on penis. Scars on both groins.

No family history obtained.

Mental condition.—Is dull and feeble-minded, mental reaction slow. Memory much impaired; after fits is pugnacious, violent, and abusive.

History of fits.—Had his first fit ten years ago. Grand mal. Epigastric aura. Mental confusion lasts about four hours.

Record of fits from admission to December 31, 1901.—Day fits, 147; night fits, 190.

Interparoxysmal alkalinity, 1·662. Alkalinity during aura, 1·26. Slight fit 10 a.m. Blood 10.15 a.m. alkalinity 1.26. Blood 12 noon alkalinity 1·48. Blood 2 p.m. alkalinity 1·59. Blood 6 p.m. alkalinity 1·59.

Case 36.—Aged 54, admitted December 13, 1900. Duration of epilepsy, five years. Bodily condition fair. Mitral systolic bruit, arteries atheromatous.

No family history obtained.

Mental condition.—Is simple and childish in manner and talk. Memory much impaired both for recent and remote events. After fits is very troublesome, and rushes wildly about the ward.

History of fits.—Developed his epilepsy about five years ago;

a week prior to his admission he had four fits. Grand mal, no aura. Mental confusion lasts about five hours.

Record of fits from admission to December 31, 1901.—Day fits, 9; night fits, 11.

Interparoxysmal alkalinity, 1·662. Strong fit at 2 p.m. Blood 2.30 p.m. alkalinity 1·0387. Blood 3 p.m. alkalinity 1·26. Blood 5 p.m. alkalinity 1·538. Blood 7 p.m. alkalinity 1·59.

Patient was subjected to the suprarenal treatment for twenty-one days; the number of fits was increased, but his mental condition improved.

Case 37.—Aged 18, admitted February 14, 1902. Duration of epilepsy, four years. Bodily condition fair.

Family history.—Father and mother alive and healthy. Paternal aunt insane, died at Banstead Asylum.

Mental condition.—Is dull and simple-minded; mental reaction slow. Memory much-impaired for recent events.

History of fits.—Had his first fit when 14 years of age. Grand mal, epigastric aura. Mental confusion lasts three hours. He has had several fits since admission, mostly nocturnal.

Interparoxysmal alkalinity, 1·48 : 1·43. Alkalinity during aura 1·18. One hour after fit, alkalinity 1·26; two hours after fit, alkalinity 1·385; four hours after fit, alkalinity 1·48; six hours after fit, alkalinity 1·538; twenty-four hours after fit, alkalinity 1·59.

Case 38.—Aged 34, admitted May 18, 1900. Duration of epilepsy, seventeen years. Bodily condition fair; is usually constipated and suffers from indigestion.

No family history obtained.

Mental condition.—Is dull and simple-minded. Memory much impaired, especially for recent events. After fits is restless, impulsive, and develops persecutory delusions.

History of fits.—Had his first fit when 17 years of age. Grand mal. Ocular aura about two minutes prior to the fit. Mental confusion lasts about four hours.

Record of fits from admission to December 31, 1901.—Day fits, 88; night fits, 35.

Interparoxysmal alkalinity, 1·538 : 1·43. Alkalinity during aura 1·26. Fit 4 p.m. Blood 4.15 p.m. alkalinity 1·12. Blood 5 p.m. alkalinity 1·26. Blood 7 p.m. alkalinity 1·43. Blood 11 p.m. alkalinity 1.48.

Case 39.—Aged 44, admitted May 29, 1899. Duration of epilepsy not known. Bodily condition fair.

No family history obtained.

Mental condition.—Is dull and feeble-minded. Memory very defective, has no idea of time. After fits is excited, impulsive and very fond of making accusations against the attendant.

History of fits.—Grand mal, epigastric aura. Mental confusion lasts about six hours.

Record of fits from admission to December 31, 1901. Day fits, 104; night fits, 134.

Interparoxysmal alkalinity, 1·48 : 1·43. Strong fit, 1 p.m. Blood 1.20 p.m. alkalinity 1·0387. Blood 3 p m. alkalinity 1·385. Blood 4 p.m. alkalinity 1·48. Blood 8 p.m. alkalinity 1·538 Blood 1 a.m. alkalinity 1·538.

Case 40.—Aged 28, admitted October 25, 1893. Duration of epilepsy, thirteen years. Bodily condition fair. Suffers from indigestion, frequently constipated.

Family history.—Father alive and healthy. Mother alive, very simple and eccentric. Mother's brother died in an asylum. Patient the only child.

Mental condition.—Is very simple and childish in manner and talk, and dirty in his habits. Memory very defective; after fits is restless and intractable.

History of fits.—Developed his epilepsy when 5 years of age. Grand mal. Mental confusion lasts about three hours.

Record of fits from admission to December 31, 1901. Day fits, 490; night fits, 998.

Interparoxysmal alkalinity 1·538 : 1·48. Fit 10 a.m. Blood 11 a.m. alkalinity 1·26. Blood 1 p.m. alkalinity 1·48. Blood 3 p.m. alkalinity 1·538. Blood 5 p.m. alkalinity 1·538. Six fits—nocturnal—3 a.m. to 4.30 a.m. Blood 11 a.m. alkalinity 1·48. Blood 12 noon alkalinity 1·59. Blood 5 p.m. 1·538.

GENERAL CONSIDERATIONS.

These results show clearly and consistently that the alkalinity of the blood in epilepsy undergoes marked variations. These variations manifest themselves in a diminution

I.—The average alkalinity during the interparoxysmal period is lower than the average of the control cases.

II.—There is a sudden and pronounced fall immediately prior to the onset of the fit.

III.—There is a further diminution after the fit is over.

I.—*The Interparoxysmal Diminution.*

All the cases studied showed this diminution with the exception of No. 35 and No. 36.

In these two cases the alkalinity was normal and varied within physiological limits. This is explained by the fact that they are senile cases with arterial degeneration and alcoholic histories, having developed their epilepsy after forty years of age, and are cases of symptomatic epilepsy.

The interparoxysmal diminution varied in several of the cases, and it was more marked in cases suffering from gastric catarrh and constipation, *e.g.*, Cases 3, 32, 37, &c. The diminution is progressive right up to the epileptic discharge, immediately prior to which there is a marked fall.

How to interpret this gradual and progressive diminution is a matter of some difficulty; the constancy of the diminution is so much in evidence that the possibility of accidental occurrence, from such concurrent diseases as anæmia, gout or rheumatism, in which the alkalinity is lowered, is ruled out (and this period in an epileptic's life is one of comparative health), and, on the other hand, the constancy with which the alkalinity is maintained within physiological limits in health is equally so well marked that the question naturally arises: What is the cause of the diminution?

(*a*) It may be explained by the gradual accumulation of toxines of an acid nature in the blood. It is interesting and instructive to note that the lowest values of alkalinity were obtained from cases suffering from gastric catarrh and constipation. Various alienists have drawn attention to the fact that gastric and intestinal troubles bear some relation to the epileptic attack, as under these conditions the fits are more frequent. Agostini (13) advanced the theory that the exciting cause is a toxin absorbed from the alimentary canal; by correcting these disorders he found much benefit, and considerable diminution in the number of fits. In gastric and intestinal catarrh there is a condition of hyperacidity both in the stomach and the intestines. The hyperacidity is due to the presence of the organic acids, lactic, acetic, and butyric acids. These acids are absorbed, pass into the circulation, and diminish the alkalinity of the blood. The writer has on several occasions raised the alkalinity in these cases by giving hydrarg. subchlor. gr. 5 and an antacid mixture. There is ample evidence to show that the alimentary canal is a fruitful source of toxines, which are absorbed into the blood, and by reacting on the organism bring forth abnormal manifestations of activity.

(*b*) It may be the result of deficient metabolism. The alkalinity of the blood is that of the body tissues generally, and the sum total of the metabolism of the body results in an alkaline reaction. Thus in epilepsy the general metabolism may be below par, with the result of a diminished value of the alkalinity of the blood, due either to a deficient amount of alkali or an excess of acid substances.

II.—*The Sudden and Pronounced Fall Immediately Prior to the Onset of the Fit.*

This phenomenon was observed in fifteen of the cases, and the blood was taken from ten seconds to two minutes before the fit. It may be regarded as the bio-chemical aura of the epileptic fit and a manifestation of some morbid change or changes taking place in the organism.

When the quantity of blood in the body (one-twelfth to one-fourteenth of the body weight), is taken into consideration, the amount of acid required to diminish the alkalinity must be relatively great, also the particular source or sources of the acid products must be qualitatively or quantitatively active. The most likely origin of these acid products are (*a*) *neuronic*; (*b*) *muscular*.

(*a*) *The neuronic origin.*—The neurones, like other cells in the body, undergo metabolic activity, and their functional activity depends upon a chemical change, a disintegration of food into chemical end products—carbonic and sarcolactic acids. The amount of acid formed must be infinitesimal; it is a case of the most highly developed cells evolving the maximum of work with the minimum formation of waste products.

The explanation of the sudden diminution by the acid products of neurone metabolism seems very fallacious. The neurones concerned in an epileptic seizure are those of the Rolandic area—a cubic inch at most on either side—and the acid products formed by their activity cannot be sufficient to lower the alkalinity of a gallon of blood, which means an enormous quantity of acid. It requires 1·662 grammes of H_2SO_4 to neutralise the alkalinity of 1,000 cc. of blood serum, and in order to neutralise the alkalinity of the total amount of blood serum, requires roughly about 4 grammes of H_2SO_4—in fact, it seems very improbable that all the cells of the cerebral cortex, say 20 grammes, can produce acid substances equal to 4 grammes of H_2SO_4. The acid products of neurone metabolism are much weaker, consequently the amount would have to be greater. On this calculation it is impossible for the neurones to produce such an amount of acid from so small a source.

Further, if this diminution in the alkalinity is due to these neuronic chemical end products, what is the condition of affairs with regard to the cerebro-spinal fluid? Compared with the volume of the blood it is scanty (the amount present is about two ounces), and the reaction would therefore necessarily be acid. But an acid medium is incompatible with the life of the neurone. The immediate surroundings are alkaline, the cerebro-spinal fluid which bathes and comes into such close contact with the neurones is alkaline, the blood is alkaline, the neurones themselves have an alkaline reaction, the sea in which they live is alkaline, and the river which flows into the sea has an alkaline reaction. This suggests that for physiological neuronic activity an alkaline medium is essential. Even an excessive, abnormal, or disordered cerebral metabolism will not account for the production of this diminution directly, and for the above reasons the neuronic origin of the sudden drop cannot be maintained.

(*b*) *The muscular origin.*—The most important metabolic tissues in the body are the muscular and the glandular. Of the two, the former is the more active; this is so because it is the most abundant, and forms about 42 per cent. of the body weight. The muscles produce by their activity the greater part of the body heat. Even during relative repose such as sleep the muscles are the seat of chemical changes, and produce a sufficient amount of heat to keep up the body temperature; also in functional paralyses where the metabolic processes in the muscles are not impaired by organic disease and the afferent and efferent channels are intact the nutrition of the muscles is relatively little impaired. The metabolism of the muscular tissue is under the control of the nervous system, and when the nervous system fails muscular metabolism is interfered with and the body temperature falls.

What has been stated above with reference to the production of heat, may be equally affirmed regarding the production of the chemical end products of muscular metabolism.

The preliminary chemical change is an oxidation, resulting in the formation of *inogen*, and the muscular contraction is a consequence of the disruption of this *inogen*, which is the first event in the response of a muscle to stimulation. It is a debatable point whether this chemical change is directly transformed into the mechanical energy which manifests itself in the muscular contraction The large bulk of muscle engaged in the violent convulsions of an epileptic seizure is an ample source for the altered reaction of the blood. That the major part of the fall should occur before the visible and violent spasms of the convulsions appear, is consequently explicable on the following considerations:—

(I.) The muscles normally, even when at rest, are the seat of metabolic activity, and produce the bulk of the body heat.

(II.) During violent exercise, the extra amount of heat produced is only a proportion of the amount of heat required to keep the body temperature within normal limits.

(III.) The chemical change is the forerunner of the muscular contraction.

(IV.) The sensori-motor areas of the cerebral cortex control the metabolism of the muscles, as is evidenced by functional paralyses, muscular tonus, and section of the spinal cord with a consequent fall in the body temperature.

It is therefore probable that there is a considerable alteration in the metabolism of the cerebral neurones, with consequent hyperexcitability and decreased inhibition some time prior to the actual epileptic discharge. This modified cortical activity brings about an increase of the metabolism which occurs prior to the visible spasms, and accounts for the sudden and pronounced diminution during this period.

III.—*The Further Diminution after the Fit is over.*

This diminution is well marked and was found in all the cases except after petit mal seizures. It is apparent soon after the fit is over, three to ten minutes, and lasts for some hours; the alkalinity gradually rises, the rise being more marked in the first hour. The return to normal varies in the different cases, but on an average takes from four to five hours. The explanation of this diminution is not far to seek. It is directly due to the acid products of muscular metabolism—carbonic and sarcolactic acids—generated during the violent tonic and clonic spasms of the muscles during the epileptic paroxysm. This phenomenon is physiological, and is seen, though in a less degree, after severe muscular exercise. The variations met with in the different cases depend upon the frequency and the number of the fits, and on the duration and the severity of the muscular twitchings. Thus, after one slight fit, the fall in alkalinity is 6°; after four fits, 8, 9 or 10°. Then again, this diminution is negligeable in cases of petit mal. These facts, together with the appearance of the fall after the spasms are over, and the gradual rise to the normal, seem to prove that the whole diminution is muscular in origin.

The relation of the diminution to the number of fits and to the duration and severity of the muscular contractions, holds good to a certain point, but the writer has taken blood from a patient who had forty fits in the short space of an hour, and from another patient after five fits, and has found the alkalinity to be of the same value, *e.g.*, ·6925. This points to a limit in the diminution.

The rapidity of return of the alkalinity to normal varies in the different cases, and in some cases, Nos. 3 and 4, the return was quick. Certain facts observed in these cases may account for the quick recovery: (*a*) free voiding of urine; (*b*) free perspiration; (*c*) leucocytosis—the greater the leucocytosis the sooner the recovery. The ultimate end of these acid products may be accounted for by excretion. They may be destroyed by the increased number of leucocytes, or they may be used as food by some of the other tissues, or neutralised by the secretions of the glands. It was also observed that the return to normal bears a relation to the mental confusion of the patient after the attack: in Case 3, where the return to normal alkalinity is comparatively rapid, the mental recovery is also rapid; in Case 1, whose mental recovery is slow, the alkalinity keeps at a low value.

The effect of drugs upon the alkalinity is transient, and it is impossible to elevate and maintain the alkalinity within physiological limits for any appreciable length of time. The bromides elevate the alkalinity even to the normal of the control cases for a certain time, but on continued administration, and even when the dose is increased, the alkalinity falls. The best results were obtained from strontii bromidi, sodii bicarb. aa. gr. 15 *ter in die*; for some time the alkalinity was maintained at a high value, but only to fall again.

In the case of No. 3, a rectal enema of potas. brom. gr. 30, chloral hydratis. gr. 20, given after twenty-four fits, raised the alkalinity from ·831 to 1·385. This was maintained for forty-five minutes, after which it dropped again to 1·0387, and gradually attained its normal value in four hours.

Suprarenal extract has apparently little effect upon the alkalinity. The effect upon the mental state was good, and all the patients subjected to the treatment recovered from their mental confusion much sooner. One of the cases, No. 4, improved considerably; usually after a fit he has a headache for some hours, but when taking suprarenal he did not have headaches. In all the cases the number and frequency of the fits were much increased, and on this account the treatment was stopped. These results are very different to those obtained by Dr. Hill (14).

The exact *rôle* which a diminution in the alkalinity of the blood plays in the production of the epileptic attack is difficult to estimate. It is of the utmost importance for any cell in the body to have a proper, adequate, and pure supply of blood, and this applies especially to the cerebral neurones, as they are extremely sensitive to a change in environment. This is well seen in the case of toxic agents circulating in the blood. As has been stated before, the conditions under which the neurones functionate is one of alkalinity, and it does not seem strange that any appreciable diminution in the alkalinity of their surroundings may bring about abnormal manifestations of activity. This applies with greater force in the case of the unstable, readily explosive, epileptic neurones. The writer has obtained good results in the treatment of epilepsy by maintaining the alkalinity of the blood within physiological limits; by doing so the number of fits is much diminished. Unfortunately it is impossible to elevate and maintain the alkalinity by the administration of drugs.

THE LEUCOCYTES.

I.—*The Interparoxysmal Period.*

There is a wide variation in the number of leucocytes. In some cases, the leucocytes were found to drop some hours before a fit. In other cases, the leucocyte count was low during the interparoxysmal period. These were cases who had frequent fits. In others, and these constituted the majority, there was a gradual drop right up to the paroxysm. A probable deduction is that the number and the activity of leucocytes depend upon the health of the epileptic in this period, that as the alkalinity of the blood diminishes and the nearer the patient is to his paroxysm, the lower is the leucocyte count, and the less the activity.

II.—*After the Fit.*

There is a distinct leucocytosis which shows itself a short time after the fit, and gradually increases, attaining its maximum from about fifty to seventy minutes after. The increase is due to the large and small hyaline cells. In the analysis of the leucocytes, the polymorphonuclear cells are diminished. The large hyaline cells are increased. The small hyaline cells are much increased. The eosinophiles are increased from two to ten hours after the attack.

The leucocytosis in the status epilepticus is not so constant, and is subject to wide variations. It takes a longer time to appear and is not so pronounced as after one individual fit. In one case, 45,000 leucocytes were counted after two fits. In another, 30,000 were counted after thirty fits in quick succession. In another case of status 12,000 white cells were counted after eighty-five fits.

The leucocytosis passes off gradually and undergoes the changes described under the interparoxysmal period. With regard to the causation, the consensus of experimental evidence seems to show that leucocytosis is to be looked upon as the reaction produced by a chemical substance circulating in the blood, and has its special mission to perform, *e.g.*, the removal or destruction of these substances. On this hypothesis, the leucocytosis following the epileptic fit may be explained. The increase of the eosinophiles some hours after the attack is much in evidence, and is also very constant, and it is probable that these cells complete the destruction of the waste products by means of their secretory functions.

Conclusions.

(1) The alkalinity of the blood in the interparoxysmal period is lower than the average of the control cases.

(2) The diminution is gradual and progressive, and is more marked in those cases suffering from gastric catarrh and constipation.

(3) There is a marked sudden and pronounced fall immediately prior to the onset of the fit.

(4) There is a further fall in the alkalinity after the fit is over; this diminution is seen from three to ten minutes after the attack.

(5) This after-diminution depends upon the duration and severity of the muscular twitching, and upon the degree of the alkalinity in the interparoxysmal period.

(6) There is a gradual return of the blood to its normal alkalinity, which takes place in five to six hours, the rise being more marked in the first hour.

(7) If the alkalinity keeps at a low value, it may determine the onset of another fit.

(8) The diminution after the fit is due to the chemical end products of muscular metabolism, *i.e.*, sarcolactic and carbonic acids, and not to substances in direct relation to the epilepsy.

(9) The diminution after a nocturnal fit takes a longer time to return to the normal than the diminution after a day fit.

(10) It is impossible to elevate and maintain the alkalinity within physiological limits for any appreciable length of time by the administration of drugs.

(11) There is a leucocytosis after a fit. The increase is due to the small hyaline cells, also to a less extent to the large hyaline cells. The polymorphonuclear cells are diminished. There is an increase in the eosinophile cells some hours after the attack.

(12) The leucocytosis is not so pronounced in status epilepticus; it diminishes with each seizure.

TABLE I.

Alkalinity of the Control Cases.

Case.	Occupation	Alkalinity.	Alkalinity.
1. J C.	Dispenser	1·662	1·662
2. W. E.	Head Attendant	1·662	1·662
3. J. D.	Attendant	1·662	1·59
4. W. B	Attendant	1·731	1·662
5. A. E. P.	Clerk	1·662	1·662
6. W. O.	Porter	1·662	1·662
7. W. H.	Porter	1·662	1·662
8. W. H. F.	Physician	1·806	1·806
9. A. B.	Head Attendant	1·59	1·662
10. R. P.	Physician	1·662	1·662
11. E. F.	Physician	1·59	1·59
12. J. N.	Attendant	1·731	1·662
13. A. H. S.	Physician	1·662	1·59
14. J. A.	Attendant	1·662	1·731
15. W. C.	Clerk	1·662	1·731
16. B. A.	Engineer	1·662	1·662
17. J. L.	Attendant	1·662	1·662
18. W. A.	Attendant	1·662	1·662
19. J. B.	Clerk	1·662	1·662
20. A. C. B.	Attendant	1·662	1·662

Table showing the Alkalinity during the Aura and Varying Periods after Paroxysm.

	Aura.	10-30 Minutes.	1 Hour.	2 Hours.	3 Hours.	4 Hours	5-12 Hours.	12-24 Hours.
Case 1, 7 fits	—	1·0387	1·26	1·385	1·43	—	—	1·43
,, 5 fits	—	–	1·18	—	1·43	1·48	1·48	—
,, 5 fits	—	·831	1·12	1·385	—	—	1·43	1·48
,, 1 fit	1·26	1 18	1·385	1·43	—	1·538	—	—
,, 2, 1 fit	—	—	—	—	1·385	—	1·538	—
,, 2 fits	—	–	1·26	1·385	1·48	—	1·59	—
,, 1 fit	1·26	1 18	1·385	1·48	—	1·538	—	—
,, 3, 8 fits	—	·831	1·26	1·385	—	1·48	—	—
,, 10 fits	—	1·18	1·385	1·26	—	1·48	—	—
,, 15 fits	—	·831	1·26	—	—	—	—	1·538
,, 4, 1 fit	—	1·0387	1·26	1·48	—	—	1·538	—
,, 5, 5 fits	—	·831	1·26	1·385	—	1·48	—	1·662
,, 1 fit	1·26	—	—	—	—	—	—	—
,, 6, 2 fits	—	1·0387	1·26	1·48	—	—	1·538	—
,, 7, 1 fit	—	1·18	1·26	—	—	—	—	—
,, 1 fit	—	1·0387	1·26	—	1·43	—	1·538	—
,, 8, 1 fit	—	1·12	1·385	1·48	—	1·538	—	—
,, 9, 1 fit	1·26	1·18	1·385	1 48	—	—	1·538	—
,, 10, 1 fit	—	—	—	—	1·385	—	1·538	—
,, 1 fit	—	1·12	—	1·385	—	—	1·538	—
,, 2 fits	—	·831	1·12	1·26	—	1·48	—	—
,, 11, 1 fit	1·385	1·18	1·385	1·48	—	1·538	—	—
,, 12, 1 fit	—	1·385	—	1·48	1·538	—	—	—
,, 3 fits	—	·831	1·12	1·26	—	1·43	1·48	—
,, 13, 2 fits	—	1·12	1·26	—	1·43	1·48	—	—
,, 14, 4 fits	1·385	1·12	—	1·385	—	1·48	1·59	—
,, 15, 1 fit	—	1·26	1·385	1·48	—	1·59	—	—
,, 16, 3 fits	—	1·12	1·26	—	1·48	—	1·59	1·59
,, 17, 2 fits	—	1·0387	—	1·385	1·48	—	1·59	—
,, 18, 1 fit	—	—	1·26	1·385	—	1·48	1·59	—
,, 19, 1 fit	—	—	1·385	1·43	—	1·48	1·59	—
,, 20, 2 fits	—	1·0387	1·26	1·43	—	1·59	—	1·59
,, 21, 1 fit	—	1·12	1·26	1·385	—	—	—	1·538
,, 22, 2 fits	—	1·12	—	1·43	—	1·43	1·59	—
,, 23, 1 fit	1·26	1·18	1·26	—	1·43	—	1·59	—
,, 24, 3 fits	—	1·0387	1 26	—	1·43	—	1·538	—
,, 25, 1 fit	1·26	1·0387	1·385	1·43	—	1·538	—	1·59
,, 26, 1 fit	1·18	—	1·26	1·385	—	1·538	—	1·59
,, 27, 2 fits	—	1·0387	1·26	1·385	—	1·538	—	1·59
,, 28, 2 fits	—	1·0387	1·26	—	1·43	—	1·538	—
,, 29, 1 fit	—	1·12	1·26	—	1·48	—	1·538	—
,, 30, 2 fits	—	1·0387	1·26	1 43	1·538	—	1·538	—
,, 31, 5 fits	—	·831	1·26	1·43	—	—	1·59	1·538
,, 32, 2 fits	—	1·18	—	1·43	—	1·48	1·59	—
,, 33, 1 fit	—	—	1·385	1·48	—	1·59	1·59	—
,, 34, 3 fits	—	1·0387	—	1·385	—	1·59	1·538	—
,, 35, 1 fit	—	1·26	—	1·48	—	1·59	1·59	—
,, 36, 1 fit	—	1·0387	1·26	—	1·538	—	1·59	—
,, 37, 1 fit	1·18	—	1 26	1·385	—	1·48	1·538	1·59
,, 38, 1 fit	1·26	1·12	1·26	—	1 48	—	1·48	—
,, 39, 1 fit	—	1·0387	—	1·385	1·48	—	1·538	—
,, 40, 1 fit	—	—	1·26	—	1·48	—	1·538	—
,, 6 fits	—	—	—	—	—	—	1·48	1·59

Cases.		Leucocytes.	Polymorphs.	Large Hyaline	Small Hyaline.	Eosinophile.	
			p.c	p c.	p.c	p c	
Case 1	..	9,500	65	6	25	3	Interparoxysmal period.
,,	..	11,000	68	5	23	4	10 minutes after 7 fits.
,,	..	21,000	60	8	29	5	60 minutes after 7 fits.
,, 2	..	14,000	60	11	25	4	60 minutes after 1 fit.
,, 3	..	9,200	68	7	22	3	Interparoxysmal period.
,,	..	19,000	60	8	30	2	40 minutes after 3 fits.
,, 4	..	10,000	70	6	21	3	Interparoxysmal period.
,,	..	12,000	62	4	30	5	4 hours after 1 fit.
,, 5	..	11,000	70	7	18	5	12 hours after 5 fits.
,, 6	..	18,000	58	8	33	2	60 minutes after 2 fits.
,, 7	..	19,000	59	9	30	3	50 minutes after 1 fit.
,, 8	..	17,000	60	10	29	1	40 minutes after 2 fits.
,, 9	..	12,400	68	6	23	3	30 minutes after 1 fit.
,, 10	..	14,000	60	8	30	3	50 minutes after 2 fits.
,, 11	..	9,000	70	7	20	3	12 hours after 1 fit.
,, 12	..	28,000	58	8	32	3	1 hour after 3 fits.
,, 13	..	20,000	58	6	39	2	1½ hours after 1 fit.
,, 14	..	11,000	61	6	25	8	6 hours after 4 fits.
,, 15	..	9,000	70	4	23	3	24 hours after 2 fits.
,, 16	..	8,000	62	6	23	9	8 hours after 1 fit.
,, 17	..	12,000	56	7	32	5	3 days after 1 fit.
,, 18	..	13,000	52	7	38	3	3 hours after 2 fits.
,, 19	..	9,000	68	8	20	4	4 days after 1 fit.
,, 20	..	14,000	57	5	34	5	4 hours after 2 fits.

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Reviews.

Traité des Maladies de la Moelle Epinière. Par J. DEJERINE, Professeur a la Faculté de Médecine de Paris, Médecin de l'Hospice de la Salpêtrière, et ANDRÉ THOMAS, ancien interne des Hopitaux de Paris, 1902.

THIS work commences with a description of the normal anatomy and physiology of the cord. The authors commit themselves definitely to the neurone theory at the outset, and, though constrained to admit that recent research has tended to throw doubts upon its unqualified acceptance, they still cling to it, partly because of the simplicity of its conception, partly on histological and pathological grounds. It might, however, be pointed out that the latter evidence is perhaps not so "irrefutable" as the authors would have us suppose.

Their description of the anatomy of the cord is somewhat disappointing; thus, for example, in describing the endogenous fibres of the posterior columns it is stated that the descending peripheral zone of Hoche and the "comma" tract of Schulze are two anatomically independent bundles of which the former alone is continued downwards as the "oval field" of Flechsig and the "triangle" of Gombault and Phillippe. Such a view, however, is not by any means universally accepted, and there are good grounds for preferring to believe that all the descending endogenous tracts in the posterior columns form one continuous system. The "septo-marginal" part of this system is not mentioned. The authors are much less dogmatic in their views as to the origin of the fibres of Gowers' tract, which, according to them, may be from the posterior, the lateral or the anterior horn. The latter group is now generally accepted as the probable source. To designate Monakow's bundle as the "faisceau pre-pyramidal (Thomas)" is surely to place an unnecessary restriction on its area, since it has been clearly shown to overlap to a considerable extent the lateral pyramidal tract. The antero-lateral descending fibres are all grouped together in a somewhat wholesale fashion, and a rather insufficient account is given of these various tracts, amongst which, for example, might have been mentioned the ventral longitudinal bundle along the ventral border of the anterior median fissure, the ponto-spinal tract or "Fissuren-strang," the vestibulo-spinal tract from Deiters' nucleus, Helweg's "Dreikantenbahn" and others.

An interesting section is that which deals with the general pathology of cord diseases. The chief etiological factors are briefly summarised as four in number:—heredity, infection, intoxication and traumatism. Before passing to the individual diseases of the cord, a section is devoted to spinal symptomatology in general. On the much disputed point as to the condition of the tendon reflexes in total transverse lesions of the cord, the authors maintain that permanent flaccid paraplegia with loss of tendon reflexes is a certain sign of complete division of the cord, spastic paralysis with increased reflexes being characteristic of an incomplete lesion. In the investigation of sensory phenomena, a good account is given of the mode of examination of the osseous sensibility, a form of sensation consisting in the vibration perceived when the base of a vibrating tuning-fork is placed on a bony surface (Egger). This feeling is apparently due to stimulation of the periosteum without intervention of the skin. Osseous anæsthesia is met with in tabes, in syringomyelia, in Brown-Sequard's paralysis (on the side of the motor paralysis), in myelitis, and, to a certain degree, in hemiplegia of cerebral origin. It is interesting to note that the normal flexor plantar reflex is considered to be a reflex of the cerebral cortex, Babinski's extensor reflex being regarded, not as a mere modification of the flexor response, but as an entirely fresh phenomenon of spinal origin. The micturition centre is still located by the authors in the conus medullaris. A considerable amount of evidence, however, has recently been brought forward by Muller[1] of Erlangen and others, indicating that the striped muscle of the neck of the bladder is alone under direct control of the cord, and that the centre for the bladder wall is located outside the central nervous system in the hypogastric plexus of the sympathetic.

The classification of affections of the spinal cord adopted by Dejerine and Thomas has the merit of simplicity. Diseases of the cord are divided into secondary and primary. The secondary affections comprise traumatism, slow compression, and the cord affections supervening in Pott's disease. Primary affections are subdivided into systematised and non-systematised. Systematised diseases comprise chronic anterior poliomyelitis, amyotrophic lateral sclerosis, tabes, Friedreich's ataxia, combined sclerosis and spastic family paraplegia. The non-systematised are again subdivided into two groups:—one group, of toxo-infectious nature, includes acute myelitis, acute and subacute anterior poliomyelitis, Landry's paralysis, and abscess of the cord; the other group, whose nature is less definitely understood, includes multiple sclerosis, hæmatomyelia, hydromyelia and syringomyelia, tumours of the cord, and, curiously enough, Little's disease.

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[1] *Deutsche Zeitsch. fur Nervenheilkunde*, 1901, Band 21, pp. 86-154.

The individual diseases are then considered in detail, and a clear account is given of the pathology, symptoms, and diagnosis of each. The authors regard most cases of "railway spine" as examples of traumatic hysteria, a certain proportion being cases of true spinal concussion. No rules, however, are laid down whereby those two can be differentiated. Attention is specially directed to post-traumatic organic affections of the cord, and it is pointed out how in certain cases a traumatism may rouse a latent predisposition, for example, to tabes, or give a point of attack for microbic infection, for new growths, or for some systemic degeneration.

The authors maintain, in opposition to Leyden and others, that chronic anterior poliomyelitis does occasionally occur independently of sclerosis of the lateral columns, and they adduce pathological evidence in support of their view. But they admit that the vast majority of cases of so-called progressive muscular atrophy are associated with changes in the lateral white columns, and should rather be classed as amyotrophic lateral sclerosis. The latter affection is one which tends to spread upwards and cause bulbar paralysis, whereas pure anterior chronic poliomyelitis is a much rarer and slower disease, which does not attack the bulbar nuclei.

In an otherwise excellent description of disseminated sclerosis it is curious to find no reference to those transient palsies of functional type which are so frequently to be observed in the early stages of the disease, and to which considerable attention has been drawn, especially by English writers.

An interesting account is given of the pathological anatomy of cavities in the cord, and examples are described both of syringomyelia proper, where the pathological cavity is distinct from the central canal, and of the rarer hydromyelia, where the central canal is itself dilated. The occasional occurrence of small neuromata in the substance of a syringomyelic cord, little nodules of interlaced young nerve-fibres, commonly in the anterior part of the cord, is emphasised, but their significance is as yet obscure.

The authors, whilst admitting that Little's disease is usually due to a bilateral cerebral lesion, maintain that the disease may also be due to a primary lesion of the cord. The reasons for this somewhat startling statement, it must be confessed, are far from convincing. Their contention is based on a single case in which a focal lesion was found in the upper cervical region, implicating the posterior cornua and the intervening posterior columns, and even in that case they figure degeneration of the pyramidal tracts above the level of the spinal lesion.

The longest section in the book is devoted to the discussion of tabes. Syphilis is regarded as its primary cause, other factors, such as nervous heredity, exposure to cold, excesses, trauma, fatigue, &c., being of secondary importance. The signs and symptoms of the disease are described in great detail, and various theories as to the nature of the underlying pathological process are discussed. The conclusion at which the authors arrive is that tabes is essentially a degenerative disease of the exogenous posterior column fibres. Why the intramedullary extent of the posterior root fibres should be so severely attacked, why the affection of the posterior roots should be so marked close outside the cord and so rapidly diminishing in intensity as the ganglion is approached, and most difficult of all, why the cells of the root ganglion itself should be practically unaffected, are questions which the authors confess themselves unable to answer.

The cord changes in pernicious anæmia are referred to as a form of "pseudo-tabes," a term which seems somewhat inadequate in view of the widespread extent of the cord degenerations that are found. No account is given of the striking clinical picture afforded by cases of acute combined sclerosis, with its characteristic sudden changes in symptomatology as the disease progresses.

The work as a whole is an excellent example of current neurological teaching in France, and well repays perusal.

PURVES STEWART.

The Treatment of Tabetic Ataxia. By Dr. H. S. FRENKEL. English edition, translated and edited by L. FREYBERGER, M.D.

DR. FREYBERGER prefaces this English edition with the information that it is not a translation, but that the language of the original has been as closely followed as is consistent with a clear exposition of the author's meaning. Whilst the desired result has, on the whole, been attained with a fair amount of success, many sentences, especially in the theoretical part of the work, remain nearly as much involved as if they had been literally translated from the German.

The detailed description of the treatment is very clearly given, and, with the help of the very numerous illustrations, should enable not only the physician but the nurse to carry out all the directions of the author with precision and intelligence.

The theory upon which Frenkel's treatment of ataxy is based assumes that the incoordination of tabes dorsalis is due to the diminution or loss of the normal sensory impulses which reach the central nervous system from the muscles, tendons and joints, and it is contended that this want can be to a large extent compensated for by the habitual use of visual impulses in place of those which are lost. This theoretical consideration is well supported by practical results, and it is now admitted by those who have utilised this system that the re-education of tabetics in movements of their limbs and trunk, under skilled supervision, can produce in suitable cases an amelioration of coordination which is unattainable by any other therapeutical measure.

Dr. Freyberger's work will have served a very useful purpose if it brings the profession in this country to recognise this fact more clearly than has hitherto been the case.

E. FARQUHAR BUZZARD.

PROCEEDINGS OF THE NEUROLOGICAL SOCIETY OF LONDON.

At a Meeting held at the Physiological Laboratory, University College, on December 4, at 8.30 p.m., the following communications were made :—

SIR VICTOR HORSLEY AND DR. BEEVOR.—*On the Pallio-tectal system of fibres* (*see* page 436).

DR. H. K. ANDERSON.—*On the part played by the dilatator in reflex pupillo-dilatation and in hippus, and on the alleged existence of irido-inhibitory fibres in the oculo-motor and cervical sympathetic nerves.*

After excision of a ciliary ganglion pupillo-dilatation was observed when light was re-admitted to the eye (the other eye being closed), if the exclusion of light was affected by a hand or cloth placed over the eye, but not if the illumination of the eye was varied without touching the animal. Light, therefore, cannot by itself vary the tone of either the sphincter or dilatator iridis through the cervical sympathetic nerve, though sensory stimulation can.

On the other hand, if a superior cervical ganglion be removed from a kitten 30 hours or more previously, the pupil on the side of the denervation may be larger than the control in dim light ("paradoxical pupillo-dilatation"), though smaller in bright light; this reversal of the difference between the two pupils (in the light of evidence that the strength of the sphincter is not affected by the denervation), must be attributed to the presence of relatively greater tone in the sound dilatator in bright light than in dim, when compared with the corresponding tone of the denervated dilatator.

This reversal of the difference between the two pupils might be affected by light causing relatively greater inhibition of the denervated dilatator through the oculo-motor nerve, but there is evidence against this explanation, since, if the paradoxical pupillo-dilatation be accentuated, as it readily may, by excitement, the pupil on the side with the denervated dilatator will remain moderately dilated even in bright sunlight, although the control is at the same time small; moreover, though both pupils react meanwhile with equal readiness to light, the paradoxically dilated pupil may remain for more than two minutes after the excitement has ceased relatively larger than the control, the disappearance of the paradoxical dilatation being, so far as I could detect, not hastened by the more brilliant illumination of the eyes. There was, therefore, no evidence in these observations that the denervated dilatator could be inhibited through the oculo-motor nerve more than the sound dilatator, or that the dilatator could be inhibited at all in this way.

The relative increase of size in the pupil on the sound side in the observation given above must, therefore, be attributed to a relative increase of tone in the sound dilatator in bright light, which is presumably caused by the increased tension of the contracting sphincter exerting greater tension upon the corresponding dilatator, and so stimulating it as in the case of a tendon-phenomenon; and in this connection also it may be noted that the same reversal of the difference between the pupils does not occur if the control sympathetic nerve is cut.

My observations also suggest that hippus is caused by rhythmic activity of the centrum cilio spinale inferius of Budge, since after excision of the ciliary ganglion the initial dilatation which followed a sensory stimulus was followed by oscillations of the pupil, and rhythmic oscillations at intervals of about four seconds were several times observed for more than five minutes continuously without sensory stimulation. In this connection the observations of Förster, Schadow, Damsch and others are discussed.

J. HERBERT PARSONS.—*On the relationship of intracranial pressure to the ocular circulation (Preliminary communication).*

The experiments were performed upon dogs, and must not, without great caution, be held to apply to higher mammals, on account of the very different blood-supply of the eye. To obviate this difficulty as far as possible the external carotid was tied so that the eye was then only supplied by the internal carotid and the circle of Willis. The eye was used as a plethysmograph, the intraocular tension being recorded. The blood pressure was recorded from the femoral artery. The animal was anæsthetised with morphia and A. C. E. mixture, and curare was given.

It was first shown that the ocular vessels act passively in all large changes of general blood pressure, so that the intraocular tension varies *pari passu* with the blood pressure. This was shown by tracings of compression of the aorta, stimulation of the vagus, vasomotor centre, splanchnics, &c., Traube-Hering curves, and drugs (nicotin, &c.).

The intracranial pressure was raised by utilising Hill's brain pressure gauge in various ways, *e.g.*, by forcing mercury into an indiarubber bag inside the cerebral cavity by saline pressure, by bleeding from the opposite carotid into the cranial cavity, &c. The curves obtained by stimulating the peripheral end of the vagus, and by drugs (nicotin, adrenalin, &c.), were compared before and after raising intracranial pressure. It was found that the change was minimal, even with pressures far above the blood pressure, and even with the opposite common carotid tied, as well as the external carotid of the same side.

Both vagi being cut, the animals usually survived with very high intracranial pressure, but the heart eventually gave out, owing to the high blood pressure induced through the stimulation of the vasomotor centre. As the blood pressure fell in these cases the intraocular tension rose enormously, probably due in part to the obstruction to venous outflow, but the exact reason this phenomenon requires further investigation.

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EDITOR.

Explanatory Note.—In consequence of an error in the paging of Part II. of vol. xxv., it will be found that pages 257 to 356 occur twice, the first time in Part II. and the second time in Part III. In the Index of the volume, the letter *a* standing after a figure refers to that page in Part II. and the letter *b* to that page in Part III.

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OF THE

Neurological Society of London,

1902,

WITH THE

Annual Report of Council, and Balance Sheet for the Year 1901.

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Neurological Society of London.

DRAFT REPORT OF COUNCIL.

FEBRUARY 6, 1902.

The Council has much pleasure in reporting the steady increase in the Members, who now amount to 220—an increase of fifty in the last ten years It has, however, to regret the loss, by death, of two members, Dr. LESLIE OGILVIE and Dr. HENRY SUTHERLAND.

It has also to lament the death of Dr. HUGHES BENNETT, who was compelled by ill-health to resign his membership a few years ago. In the early days of the Society Dr. HUGHES BENNETT was one of its most active and useful members; he was Secretary during the years 1886 and 1887, and Member of Council from 1888 to 1891.

The Presidential Address was given by Dr. MICKLE, who took for his subject "Mental Wandering." In June, on the invitation of Professor DRESCHFELD and other members living in Manchester, the Society held a meeting in that city—the third time it had met out of London. At the meeting most successful pathological, clinical, and experimental demonstrations were arranged and were attended by a very large number of members and visitors; and in the evening the Society was hospitably entertained to dinner by the Manchester members. The meeting was an unqualified success, and the Council desires to record its grateful thanks to all concerned, particularly to Mr. THORBURN, Professor STIRLING, Dr. JUDSON BURY and Dr E. S. REYNOLDS, who formed the Reception Committee.

Under the Editorship of Dr. PERCY SMITH, "Brain," the organ of the Society, continues to hold a leading place among neurological publications The cost of illustrating papers in "Brain" had of recent years been increasing to such an extent that it was absorbing most of the income of the Society. The Council has therefore been compelled to put a limit to the amount which can be paid by the Society for the illustration of each paper.

Chiefly owing to this increased expenditure in illustration, the resources of the Society have been somewhat strained. Bills for over seventy pounds for illustrations occurring during 1900 were not sent in to the Treasurer until the present financial year The payment of these bills leaves the finances of the Society at the end of this year in a state of temporary embarrassment, as is shown on the appended Balance Sheet; but, with retrenchment in expenditure, the Council believes that at the end of twelve months they will again be in a satisfactory condition. The Council proposes to increase the income of the Society by raising the annual subscription to a guinea instead of one pound.

In the Report for 1896 it was announced that Sir WILLIAM BROADBENT had generously given a grant of thirty-six guineas towards the expenses of preparing an Index of "Brain." The work was entrusted to a number of different workers, and the subjects indexed on cards. Owing to several unavoidable circumstances, the arrangement of these cards for the formation of the Index was delayed. Early in the present year the cards were handed to the present Editor for arrangement and publication, but owing to the want of any uniformity of plan on the part of the different indexers, the preparation of the Index for the press by Dr. PERCY SMITH has involved an immense amount of labour. The final proofs of the Index, which deals with the first twenty-three volumes of "Brain," *i.e.*, down to the end of 1900, have been corrected, and the volume will very shortly be issued by Messrs. Macmillan, from whom Members can obtain it at a reduced price. The Council desires once more to express its warmest thanks to Sir WILLIAM BROADBENT; and also to Dr. PERCY SMITH for the pains and care which he has taken to make the volume a useful work of reference to neurologists.

An abstract of the Proceedings of the Society appended to this Report shows the character and value of the work of the Society during the past year.

Proceedings of the Society during the year 1901.

February 14.—Dr. W. J. MICKLE, Inaugural Address, "Mental Wandering."

March 21.—Dr. F. E. BATTEN, "Four cases of congenital ataxia in children." Dr. FARQUHAR BUZZARD, "Atrophy of arms with anæsthesia over distribution of the first dorsal root." Dr. RISIEN RUSSELL, "Syringomyelia with Charcot-joint." Dr. W. A. MARRIS, "Two cases resembling disseminated sclerosis." Dr STILL, "A case of paramyoclonus multiplex."

May 9.—Dr. JOHN TURNER, "A method of staining nervous tissues in methylene blue." Dr. MICHELL CLARKE, (1) "A case of pachymeningitis of the spinal cord", (2) "Changes in the posterior columns of the spinal cord in a case of pernicious anæmia"; (3) "Tumour of the right optic thalamus." Dr. WAKELIN BARRATT, "Changes in the nervous system in a case of old-standing amputation." Dr. FREDERICK BATTEN, "Specimens from three cases of infantile paralysis."

June 22.—An extraordinary meeting of the Society was held at Manchester. *Specimens were shown by:* Dr. A. BRUCE, (1) Photogravures of each segment of the normal spinal cord; (2) Photographs and sections of—(*a*) Hæmorrhage into spinal cord, (*b*) Cavities in cord above a spina bifida, (*c*) Syringo-myelia, (*d*) Progressive muscular atrophy and amyotrophic lateral sclerosis, (*e*) Glioma of pons, (*f*) Syphilitic meningo-myelitis; (3) Photographs from a case of complete paralysis of the brachial plexus. Dr. JUDSON BURY, (1) Porencephalus; (2) Hydrocephalus; (3) Acromegaly. Professor SHERIDAN DELÉPINE, (1) Actinomycotic abscess of brain; (2) Experimental arsenical neuritis; (3) Other lesions of the central nervous system. Professor J. DRESCHFELD, (1) Spinal cord in ataxia paraplegia; (2) Spinal cord in disseminated myelitis; (3) Casts and photographs. Mr. W. MILLIGAN, (1) A portable surgical motor. Dr F. CRAVEN MOORE, (1) Multiple gummata of brain and spinal cord; (2) Hæmorrhagic meningo-encephalitis (influenza) (Dr. DRESCHFELD's case); (3) Metatastic calcification of vastus internus tendon with Charcot's arthropathy (Dr. DRESCHFELD's case); (4) Specimens from poisoning by arsenical beer; (5) Cerebral tumours. Dr. F. W. MOTT, Effects of bitulin, abrin, absinthe, and picrotoxin upon nerve-cells. Drs. ORR and ROWS, (1) Types of nerve-cells in the spinal ganglia of rabbits; (2) Nerve-cells in the spinal ganglia of man and different forms of chromatolysis in general paralysis of the insane; (3) Spinal ganglion cells in acute mania, showing vacuolation. Dr. E. S. Reynolds, Photographs of neurological cases, including a series illustrative of the recent epidemic of arsenical poisoning. Professor C. S. Sherrington and Dr. E. E. Laslett, Microscopical sections (*infra*). Professor W. Stirling, (1) Exhibits to illustrate some of the phenomena of stereoscopic vision, (2) An original experiment on binocular colour vision; (3) An experiment to show how the actual size of the pupil is affected by the cornea; (4) View of the interior of the frog's heart to show the arrangement of its muscular fibres; (5) Enucleation of the eyeball and removal of the floor of the orbital cavity, showing position of soft palate in phonation; (6) Simple method of examining the retina in a living rabbit; (7) A classical experiment concerning the discovery of the capillaries (Malpighi, de pulmonibus) and a modern one, (8) Some optical illusions; (9) Some experiments in physiological optics; (10) Lantern slides of some distinguished physiologists; (11) Original picture of the Kircher's "Experimentum Mirabile"; (12) Some anaglyphs, (13) The structure of some electrical organs; (14) Complete injection of the blood-vessels of the eyeball of a small animal. Dr. E. F. Trevelyan, (1) Various specimens showing the value and permanency of Laskowsky's method; (2) Specimens preserved in Kaiserling's fluid; (3) Tuberculous tumour of the brain, meninges and skull; (4) Intact pia-arachnoid from a fœtus. Professor A. H. Young, Stereoscopic photographs of the brain. Dr. W. B. Warrington, (1) Sections of unilateral optic atrophy; (2) Photographs of Tooth's peroneal atrophy. Dr. R. T. Williamson, (1) Two cerebellar tumours with photographs; (2) Microscopical specimens of—(*a*) Progressive muscular atrophy, (*b*) Early tabes, (*c*) Acute anterior poliomyelitis of the adult. (*d*) Myelitis in the distribution of the anterior and of the posterior spinal arteries, (*e*) Peripheral nerves in multiple neuritis, (*f*) Spinal syphilis—thrombosis, hæmorrhage and myelitis, (*g*) Retro-bulbar optic neuritis associated with cancer of stomach. *Clinical cases were shown by*: Dr. Ashby. Dr. Judson Bury, (1) Syringomyelia with hemianæsthesia, (2) Sensory aphasia (two cases); (3) Ophthalmoplegia, (4) Hemiplegia, hemianæsthesia and impairment of special senses on one side. (5) Cases of muscular atrophy; (6) Hæmorrhage (?) into the spinal cord. Dr. Dreschfeld (1) Thomsen's disease (two cases); (2) A family (five cases) showing various stages of Erb's muscular dystrophy. Dr. Haring. Dr. Harris, Unusual defect in the skull (? cephalhydrocele) with both hysterical and epileptic attacks. Dr. Dixon Mann. Dr. E. S. Reynolds, (1) Locomotor ataxia with multiple joint lesions; (2) Unilateral lesion of the spinal cord (two cases), (3) Ataxia paraplegia (disseminated sclerosis ?); (4) Chronic anterior poliomyelitis. Dr. R. T. Williamson, (1) Unilateral tremor most marked in leg (? paralysis agitans); (2) Very early tabes with knee-jerks present (two cases); (3) Disseminated sclerosis following influenza. Dr. Williamson and Dr. P. Tytler, Hydatid of spine (extra-dural) with compression myelitis, operation with gradual improvement for twelve months. Professor C. S. Sherrington and Dr. E. E. Laslett gave a short "Note on the third, fourth and sixth cranial nerves." Drs. Alexander Bruce, Mott and Orr gave lantern demonstrations of specimens shown in the Histological Laboratory (*supra*). Professor Wm. Stirling showed (1) Some classical experiments bearing on neuro-physiology, and one new experiment; (2) Malapterurus electricus (living) and its mode of feeding.

October 31.—Dr. FERRIER, "Case of successful removal of a cerebellar tumour." Dr FERRIER and Dr. ALDREN TURNER, "Case of successful removal of a cerebral tumour." Dr. ROBERT HUTCHISON, "Unilateral incoördination with inability to rotate the eyes downwards in a mentally defective boy." Dr. BEEVOR, "A case of affection of the first dorsal nerve." Dr. HEAD, (1) "A case of muscular atrophy in a young woman, probably of neuritic origin"; "A case for diagnosis." Dr. BATTEN, "Spasmodic movements in the limbs of an infant." Dr. MUSKENS demonstrated lantern slides to illustrate the segmental disturbances of sensation in cases of tabes dorsalis and epilepsy.

December 4 was devoted to psycho-physical methods, and Dr. RIVERS gave a demonstration (1) On methods for estimating mental fatigue and practice; (2) On methods of measuring mental illusions. Dr. F. SMITH showed an apparatus for measuring reaction time.

BALANCE SHEET, 1901.

NEUROLOGICAL SOCIETY.

Cr. **Dr.**

RECEIPTS.	£	s	d.
To Balance	66	1	4
Subscriptions	230	5	6
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Hire of Examination Hall	5	5	0			
Meeting at Manchester	1	12	0			
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Balance at Bankers	16	5	7
	63	14	7
Deficit	55	12	5
	£119	7	0

LIABILITIES.	£	s.	d.
By Messrs. Macmillan's Account for publishing "Brain"	119	7	0
	£119	7	0

Audited and found correct, December 20, 1901, { LEONARD GUTHRIE,
PURVES STEWART

CHARLES E. BEEVOR, *Hon. Treasurer.*

RULES.

1.—The Society shall be called the NEUROLOGICAL SOCIETY OF LONDON.

2.—The objects of the Society shall be to promote the advance of Neurology and to facilitate intercourse amongst those who cultivate it, whether from a Psychological, Physiological, Anatomical, or Pathological point of view.

3.—The Society shall consist of Ordinary, Corresponding, and Honorary Members.

4.—Any one engaged in researches bearing on Neurology, or manifesting interest in such researches, shall be eligible for the Ordinary Membership.

5.—Men of distinction in Science, who have contributed to the advancement of Neurology, shall be eligible for the Honorary, or for the Corresponding Membership

6.—The number of Honorary Members shall be limited to six, and that of Corresponding Members to twelve

7.—Honorary and Corresponding Members shall have the right of attending the Meetings of the Society and of taking part in them.

8—Honorary and Corresponding Members shall be elected by the Society on the recommendation of the Council

9.—Candidates for Ordinary Membership shall be recommended by at least three Members of the Society, who shall append their names to a printed form supplied by the Secretaries to any person seeking Membership

10.—The Council shall nominate candidates for election into the Society as Ordinary Members from among persons so recommended.

11.—The names of Candidates nominated by the Council shall be submitted to the next Meeting of the Society, and shall be balloted for at the next subsequent meeting, one black ball in ten excluding.

12.—The Annual Subscription of an Ordinary Member shall be One Guinea, due in advance.

13.—The Treasurer shall send to each Member, shortly before the Annual General Meeting, a notice reminding him that his Subscription becomes due on that day.

14.—Non-payment of the Subscription within twelve months after it is due, shall be considered as equivalent to resignation.

15.—The Council shall consist of a President, two Vice-Presidents, two Secretaries, one Treasurer, and ten Councillors.

16.—Five Members of the Council shall form a quorum.

17.—The office of President shall be tenable for one year, and be entered upon at the beginning of each year by the Senior Vice-President

18.—The office of Vice-President shall be tenable for two years, one Vice-President being elected every year.

19.—The Secretaries and Treasurer shall be elected annually with eligibility for re-election.

20.—The Councillors shall be elected for one year, and not more than eight shall be eligible for re-election to the same office during the following year.

21.—One full week before the Annual General Meeting, the Secretaries shall send to each Member a balloting paper containing the names of the Officers and Councillors whom the Council nominate for the ensuing year.

22.—The Society shall elect the Council by ballot, each Member, however, being at liberty to substitute other names for any of those upon the list.

23.—There shall be six Ordinary Meetings annually, of which the first held in each year shall be the Annual General Meeting.

24.—Notices of each meeting, and of the subjects to be considered, shall be sent by the Secretaries to each Member of the Society at least one week before the meeting

25.—Special Meetings shall be held at the option of the Council, or at the request, in writing, of twenty Members.

26.—The President shall have the power of inviting any person to attend and to take part in the scientific work of the meeting

27.—If at any time the Council shall be of opinion that the interests of the Society require the expulsion of a Member, they shall submit the question to a special General Meeting, at which, if more than one-half of the Members of the Society vote, by ballot as usual, for the expulsion of the Member, his subscription for the current year shall be returned to him, and he shall thereupon cease to be a Member of the Society

28.—The Council shall draw up and submit for the approval of the Society, supplementary rules regulating the dates, places, and character of the meetings, shall propose special subjects for investigation by the Society, and shall nominate sub-committees for the methodical carrying out of such investigations. They shall decide, from time to time, on the form of publication which its proceedings are to assume

29.—No alteration shall be made in the present rules, excepting at the Annual Meeting, or at a Special Meeting convened for the purpose, and unless it be proposed by the Council, or in writing by at least twenty Members. the usual notice be given of the proposed change to every Member before the meeting at which it is to be brought forward.

Each Member receives quarterly, from the beginning of the year in which he is elected, a copy of "BRAIN; a Journal of Neurology," the organ of the Society, and edited for it by R. Percy Smith, M.D., F.R.C.P.

HONORARY MEMBERS.

Mr. Herbert Spencer, London.
Professor Wundt, Leipzig.
„ Hitzig, Halle
Sir Samuel Wilks, Bart., London

CORRESPONDING MEMBERS.

Professor Erb, Heidelberg.
„ Golgi, Pavia.
„ Goltz, Strasburg.
„ Grasset, Montpellier.
„ Jolly, Berlin.
„ Luciani, Rome.
„ Munk, Berlin.
„ Obersteiner, Vienna.
„ Retzius, Gustaf, Stockholm.
„ Ribot, Paris.
Dr. Weir Mitchell, Philadelphia

LIST OF PRESIDENTS FROM THE FOUNDATION OF THE SOCIETY.

1886	J. Hughlings Jackson, M.D., F.R.S.
1887	Sir Samuel Wilks, Bart., M.D., F.R.S.
1888	Sir James Crichton-Browne, M.D., F.R.S.
1889	Jonathan Hutchinson, F.R.S.
1890	Thomas Buzzard, M.D.
1891	John S. Bristowe, M.D., F.R.S.
1892	H. Charlton Bastian, M.D., F.R.S.
1893	Edward A. Schafer, F.R.S.
1894	David Ferrier, M.D., F.R.S
1895	Sir William H. Broadbent, Bart., M.D., F.R.S.
1896	Alexander Hill, M.A., M.D.
1897	George H. Savage, M.D.
1898	Victor Horsley, M.B., F.R.C.S., F.R.S.
1899	W. H. Gaskell, M.D., F.R.S.
1900	Augustus Waller, M.D., F.R.S.
1901	W. Julius Mickle, M.D.
1902	Herbert William Page, M.A., F.R.S.

LIST OF HUGHLINGS JACKSON LECTURERS.

1897	J. Hughlings Jackson, M.D., F.R.S.
1900	Professor Eduard Hitzig, Halle.

*** Members are requested to communicate with the Secretaries when corrections are necessary.

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EXPLANATION OF ABBREVIATIONS.

O.M., Original Member.	Tr., Treasurer.
Pres., President.	Sec., Secretary.
V.-P., Vice-President.	C., Member of Council.

H.J.L., Hughlings Jackson Lecturer.

ORDINARY MEMBERS.

Elected	
1899	Abrahams, Bertram, M.B., M.R.C.P., 14, Welbeck Street, W.
1892	Alexander, Robert Reid, M.D., The Asylum, Hanwell, W.
1897	Anderson, H. Kerr, M.B., B.Sc., Whitefield, Great Shelford, Cambs.
1894	Andriezen, W. Lloyd, M.D., 7, Apsley Terrace, Acton, W.
1891	Ballance, C. A., M.S., F.R.C.S., 106, Harley Street, W. (C., 1897-1900.)
O.M.	Barlow, Sir Thomas, Bart., M.D., F.R.C.P., 10, Wimpole Street, W.
1897	Barratt, J. O. Wakelin, M.D., F.R.C.S., Pathological Laboratory, West Riding Asylum, Wakefield.
O.M.	Bastian, H. Charlton, M.D., F.R.C.P., F.R.S., 8a, Manchester Square, W. (Pres., 1892; V.-P., 1891; C., 1886-89, 1893-95.)
1897	Batten, Frederick E., M.D., F.R.C.P., 33, Harley Street, W.
O.M.	Beach, Fletcher, M.B., F.R.C.P., Winchester House, Kingston Hill, Surrey.
,,	Beevor, C. E., M.D., F.R.C.P., 135, Harley Street, W. (Tr., 1894-1902, C., 1893.)
1888	Birt, Ernest, M.D., West Riding Asylum, Wakefield.
1898	Bolton, Joseph Shaw, M.D., B.S., B.Sc., Claybury Hall, Woodford, Essex.
1896	Bond, C. Hubert, M.D., D.Sc., London County Asylum, Bexley, Kent.
1890	Bond, J. W., M.D., B.S., 26, Harley Street, W.
1892	Bowlby, Anthony A., F.R.C.S., 24, Manchester Square, W.
1898	Boyce, Rupert W., M.B., University College, Liverpool.
,,	Bradbury, John B., M.D., F.R.C.P., 4, St. Peter's Terrace, Cambridge.
1889	Bradford, J. R., M.D., D.Sc., F.R.C.P., F.R.S., 8, Manchester Square, W.
O.M.	Bramwell, Byrom, M.D., F.R.C.P.Ed., 23, Drumsheugh Gardens, Edinburgh. (C., 1894.)
1899	Bramwell, Edwin, M.B., C.M., M.R.C.P., 2, Randolph Place, Edinburgh.
1895	Bramwell, John Milne, M.B., C.M., 15, Stratford Place, W.
1892	Bristowe, Hubert Carpenter, M.D., Wrington, Somerset.

Elected

O.M. **Broadbent**, Sir **Wm. H.**, Bart., M.D., F.R.C.P., F.R.S., 84, Brook Street, W. (Pres., 1895; V.-P., 1893; C., 1886-87, 1896.)

1894 **Brodie**, T. **Gregor**, M.D., 55, Marlborough Mansions, West Hampstead, N.W.

1897 **Brown**, H. H., M.D., F.R.C.S., 22, Museum Street, Ipswich.

1888 **Brown**, **Sanger**, M.D., 100, State Street, Chicago.

O.M. **Bruce**, **Alex.**, M.D., F.R.C.P.Ed., 8, Ainslie Place, Edinburgh. (C., 1895.)

,, **Bruce**, J. **Mitchell**, M.D., F.R.C.P., 23, Harley Street, W.

1898 **Bruce**, **Samuel Noble**, M.R.C.S., 15, Queensboro' Terrace, Hyde Park, W.

O.M. **Brunton**, Sir T. **Lauder**, M.D., F.R.C.P., F.R.S., 10, Stratford Place, W. (C., 1896-98.)

1895 **Bryan**, **Frederick**, M.B., Horton Manor Asylum, Banstead Downs, Surrey.

,, **Bryant**, **John Henry**, M.D., F.R.C.P., 8, Mansfield Street, Portland Place, W.

1890 **Bury**, **Judson Sykes**, M.D., F.R.C.P., 10, St. John Street, Manchester.

1900 **Buzzard**, E. **Farquhar**, M.B., M.R.C.P., 38, Harley Street, W.

O.M. **Buzzard**, **Thomas**, M.D., F.R.C.P., 74, Grosvenor Street, W. (Pres., 1890, V.-P., 1888-89; C., 1886-87, 1891-95.)

1898 **Caley**, H. A., M.D., F.R.C.P., 24, Upper Berkeley Street, W.

,, **Campbell**, **Harry**, M.D., F.R.C.P., 23, Wimpole Street, W.

1887 **Cattell**, J. **McK.**, M.A., Ph.D., Columbia College, New York, U.S.A.

1899 **Chambers**, **James**, M.A., M.D., The Priory, Roehampton.

1891 **Clarke**, J. **Michell**, M.D., F.R.C.P., 28, Pembroke Road, Clifton, Bristol.

1892 **Cole**, **Robert Henry**, M.D., M.R.C.P., 48, Upper Berkeley Street, Portman Square.

1899 **Collier**, J. S., M.D., B.Sc., M.R.C.P., 57a, Wimpole Street, W.

1890 **Colman**, W. S., M.D., F.R.C.P., 22, Wimpole Street, W. (Sec., 1899-1902.)

,, **Corner**, **Harry**, M.D., Brook House, Southgate, Middlesex.

1899 **Coupland**, **Sidney**, M.D., F.R.C.P., 16, Queen Anne Street, W.

1901 **Cox**, **Joshua John**, M.D., St. Ronan's, Clarendon Road, Eccles, Manchester.

1901 **Craig**, **Maurice**, M.D., M.R.C.P., Bethlehem Royal Hospital, S.E.

1895 **Davidson**, **Andrew**, M.D., The County Asylum, Dorchester, Dorset.

1897 **Dawson**, **William** R., M.D., F.R.C.P.I., Farnham House, Finglas, Co. Dublin, Ireland.

1894 **Dean**, H. **Percy**, M.S., F.R.C.S., 69, Harley Street, W.

1898 **Dodd**, **Henry Work**, F.R.C.S., 136, Harley Street, W.

O.M. **Dreschfeld**, **Julius**, M.D., F.R.C.P., 3, St. Peter's Square, Manchester. (V.-P., 1898-99.)

,, **Drummond**, **David**, M.D., 6, Saville Place, Newcastle-on-Tyne.

1892 **Dupuy**, **Eugene**, M.D., 53, Avenue Montaigne, Paris.

Elected

1901 Edridge-Green, F. W., M.D., F.R.C.S., Hendon Grove, Hendon, N.W.

1899 Fawcett, John, M.D., M.R.C.P., 26, St. Thomas Street, S.E.

O.M. Ferrier, David, M.D., F.R.C.P., F.R.S., 34, Cavendish Square, W. (Pres., 1886; V.-P., 1892-3; C., 1886-90-95.)

,, Gaskell, W. H., M.D., F.R.S., The Uplands, Great Shelford, Cambs. (Pres , 1899; V.-P., 1897-98; C., 1896, 1900.)

,, Gee, Samuel J., M.D., F.R.C.P., 31, Upper Brook Street, W.

,, Godlee, R. J., M.B., F.R.C.S., 19, Wimpole Street, W.

1899 Goodall, Edwin, M.D., M.R.C.P., Joint Counties Asylum, Carmarthen.

1898 Goodliffe, Jno. Henry, M.D.Aberd., 802, High Road, Lower Tottenham.

1897 Gossage, Alfred Milne, M.B., M.R.C.P., 54, Upper Berkeley Street, W.

1892 Gotch, Francis, M.A., F.R.S., The Lawn, Banbury Road, Oxford.

1893 Grant, J. Dundas, M.D., F.R.C.S., 18, Cavendish Square, W.

O.M. Gunn, R. Marcus, M.B., F.R.C.S., 54, Queen Anne Street, W. (C., 1899-1900.)

1895 Guthrie, Leonard, M.D , F.R.C.P., 15, Upper Berkeley Street, W.

1901 Hall, W. Hamilton, M.R.C.S., Fordcombe, Tunbridge Wells.

1893 Halliburton, William Dobinson, M.D., F.R.C.P., F.R.S , Church Cottage, 17, Marylebone Road, N.W.

O.M. Hamilton, D. J., M.B., F.R.S.E., University, Aberdeen.

1898 Hanbury, William R., M.R.C.S., L.R.C.P., West Ham Borough Asylum, Goodmayes, Ilford.

1897 Harris, Wilfred J., M.D., M.R.C.P., 37, Queen Anne Street, W.

1898 Hartley, W. Darley, M.D., M.R.C.P., Park House, Kloof Street, Cape Town, South Africa.

,, Haslett, John Hanfield, M.R.C.S., L.R.C.P., Halliford House, Sunbury-on-Thames.

1891 Hawkins, Herbert Pennell, M.D., F.R.C.P., 56, Portland Place, W.

O.M. Haycraft, J. B., M.D., D.Sc., F.R.S.E., 1, St. Andrew's Place, Cardiff.

1891 Head, Henry, M.D., F.R.C.P., F.R.S., 61, Wimpole Street, W. (C., 1900; Sec., 1901-1902.)

O.M. Hill, Alex., M.A., M.D., Downing Lodge, Cambridge. (Pres., 1896; V.-P., 1895; C., 1892-94.)

O.M. Horsley, Victor, F.R.C.S., F.R.S., 25, Cavendish Square, W. (Pres., 1898, V.-P., 1896-97; C., 1892-93, 1899.)

1889 Huggard, William R., M.D., F.R.C.P., Davoz Platz, Switzerland.

1896 Hulme, George Frederick, M.B., C.M., South View, Montague Road, Felixstowe.

1889 Humphry, Laurence, M.D., M.R.C.P., Lensfield, Cambridge.

1901 Hunter, William, M.B., C.M., London Hospital Medical College, E.

O.M. Hutchinson, Jonathan, F.R.C.S., F.R.S., 15, Cavendish Square, W. (Pres., 1889; V.-P., 1887-88; C., 1886, 1890.)

1889 Hyslop, T. B., M.D., C.M., Bethlem Royal Hospital, Lambeth, S.E.

Elected

O.M. Jackson, J. Hughlings, M.D., F.R.C.P., F.R.S , 3, Manchester Square, W. (Pres., 1886; H.J.L., 1897; C., 1887, 1892.)

,, Jessop, W. H , M.B., F.R.C.S., 73, Harley Street, W.

1895 Johnston, George, M.D., M.R.C.P., 3, Montagu Place, Montagu Square, W.

1892 Jones, Henry Lewis, M.D., F.R.C.P., 61, Wimpole Street, W.

1894 Jones, Robert, M.D., F.R.C.S., Claybury Asylum, Woodford, Essex.

1901 Kelynack, T. N., M.D., M.R.C.P., 53, Harley Street, W.

1894 Kidd, Percy, M.D , F.R.C P., 60, Brook Street, W.

1896 Langdon, F. W., M.D., Cincinnati, Ohio, U.S.A.

1898 Langdon-Down, Reginald L., M.B., M.R.C.P., 47, Welbeck Street, W.

O.M. Langley, J. N., M.A., D.Sc., F.R.S., Trinity College, Cambridge. (V.-P., 1901-1902; C., 1898-99.)

1888 Lawford, J. B., M.D., F.R.C.S., 99, Harley Street, W. (C., 1902.)

O.M. Lees, D. B., M D., F.R.C.P., 22, Weymouth Street, W. (C., 1901-1902)

1897 Lewis, H. Wolseley, M.R.C.S., L.R.C.P., London County Asylum, Banstead, Surrey.

1901 Little, E. Graham, M.D., M.R.C.P., 61, Wimpole Street, W.

1897 Loewenthal, Max, M.D., M.R.C.P., 126, Princes' Road, Liverpool.

1899 Lord, John R., M.B., C.M., London County Asylum, Bexley, Kent.

1898 MacCormac, John M'Gee, M.D., 31, Victoria Place, Belfast.

,, McAldowie, Alexander M., M.D., 6, Brook Street, Stoke-on-Trent.

1891 Macdonald, Peter William, M.D., C.M., The County Asylum, Dorchester, Dorset.

,, Mackenzie, Hector William Gavin, M.D., F.R.C.P., 34, Upper Brook Street, Grosvenor Square, W.

O.M. Mackenzie, Stephen, M.D., F.R C.P., 18, Cavendish Square, W. (C , 1896-98.)

1896 Mackintosh, Ashley W., M.A., M.D., 9, Bon Accord Square, Aberdeen.

1899 MacLulich, Peers, M.D., B.Ch., Joint Counties Asylum, Carmarthen.

1889 Macphail, S. R., M.D., Borough Asylum, Rowditch, Derby.

O.M. Maguire, Robert, M D., F.R C.P , 4, Seymour Street, W. (Sec., 1890-93; C., 1893-96.)

,, Mann, J. Dixon, M.D., F.R.C.P., 16, St. John's Street, Manchester.

,, Marris, W. A., M.D., The Vron, Ascot Road, Moseley, Birmingham

1894 Martin, Sidney, M.D., F.R.C P., F.R.S., 10, Mansfield Street, W.

1891 May, W. Page, M.D., M.R.C.P., Helouan, Cairo, Egypt.

1890 Menzies, William Francis, M.D., B.Sc., M.R.C.P., Cheddleton Asylum, Leek, Staffordshire.

O.M. Mercier, C., M.B., M.R.C.P., Flower House, Southend, Catford, S E. (C., 1899-1902.)

Elected
1897 Meyer, Adolf, M.D., Clark University, Worcester, Mass., U S.A.
O.M. Mickle, W. Julius, M.D., F.R.C.P., Grove Hall Asylum, Bow, E. (Pres., 1901; V.-P., 1900; C., 1895-97, 1902.)
1895 Moore, Norman, M.D., F.R.C.P., 94, Gloucester Place, W.
O.M. Morris, Malcolm, F.R.C.S.Ed., 8, Harley Street, W.
1888 Mott, F. W., M.D., F.R.C.P., F.R.S., 25, Nottingham Place, W. (Sec , 1894-98; C., 1899-1902.)
1899 Mould, Gilbert E., M.R.C.S., L.R.C.P., The Grange, nr. Rotherham,
1901 Mould, George Wm., M.R.C.S.; Cheadle Royal Asylum, Manchester.
1894 Murray, George R , M.A., M.D., F.R.C.P., 11, Ellison Place, Newcastle-on-Tyne.
1889 Murray, H. Montague, M.D., F R.C.P., 25, Manchester Square, W.

O.M. Nettleship, Edward, F.R.C.S , Shottermill, Haslemere, Surrey.
,, Nicolson, David, C.B., M.D., M.R.C.P.Ed., Balgownie, Guildford, Surrey.
1888 Niermeyer, J. H. H., M.D., Amsterdam.
,, Norman, Conolly, F.R.C.P.I., F.R.C.S.I., St. Dymphna's, N. Circular Road, Dublin.

1887 Ogilvie, George, M.B., M R.C.P., 22, Welbeck Street, W.
,, Oliver, Thomas, M.D., F.R.C.P., 7, Ellison Place, Newcastle-on-Tyne,
O.M. Orange, Wm , C.B.; M.D., F.R.C.P , The Bryn, Godalming, Surrey.
,, Ord, W. M., M.D., F.R.C.P., Hurstbourne Tarrant, Andover. (C., 1893-94.)
,, Ormerod, J. A., M.D., F.R.C.P., 25, Upper Wimpole Street, W. (C., 1895-97.)
,, Orr, David, M.B., County Asylum, Prestwich, Manchester.

,, Page, Herbert William, M.A., F.R.C.S., 146, Harley Street, W. (Pres., 1902; V -P., 1900-1; C., 1891-92.)
1895 Parkinson, John Porter, M.D., M.R.C.P., 57, Wimpole Street, W.
1901 Parsons, John Herbert, M.B., B.Sc., 28, Great Ormond Street, W.C.
1901 Passmore, E. S., M.D., M.R.C.P., Banstead Downs, Sutton, Surrey.
1896 Paterson, Donald Rose, M.D., M.R.C.P , 15, St. Andrew's Crescent, Cardiff.
1895 Pinder, George, M.D., St. Swithin's, Worthing.
1899 Piper, Francis P., M.B., M.R.C.S., L.R.C.P., Claybury Asylum, Woodford, Essex.
1888 Pitt, G. N., M.D., F.R.C.P., 15, Portland Place, W.
O.M. Poore, G. Vivian, M.D., F.R.C.P., 24a, Portland Place, W. (C., 1898-99.)
,, Purves, W. Laidlaw, M.D., 20, Stratford Place, W.

1899 Rambaut, Daniel F., M.D., B.Ch., Richmond District Asylum, Dublin.
1894 Ransom, William B., M.D., F.R.C.P., The Pavement, Nottingham.

Elected

1890 RAYNER, HENRY, M.D., M.R.C.P.Ed., 16, Queen Anne Street, W.

O.M. REID, E. W., M.B., F.R.S., University College, Dundee.

1897 REISSMANN, CHARLES H., M.B., B.Sc., Knutsford, Glenelg, South Australia.

1893 RENNIE, GEORGE E., M.D., M.R.C.P., College Street, Sydney.

1895 REYNOLDS, ERNEST S., M.D., F.R.C.P., 2, St. Peter's Square, Manchester.

1892 RICHARDS, JOSEPH PEEKE, M.R.C.S., 6, Freeland Road, Ealing, W.

1891 RIVERS, W. H. R., M.A., M.D., F.R.C.P., St. John's College, Cambridge. (C., 1897-98.)

1898 ROBERTSON, WILLIAM FORD, M.D., 7, Hill Square, Edinburgh.

1892 ROWE, EDMUND LEWIS, L.R.C.P., L.R.C.S., Borough Asylum, Ipswich.

1901 ROWS, R. G., M.D., County Asylum, Whittingham, Manchester.

1892 RUFFER, MARC ARMAND, M.D., Alexandria, Egypt.

1889 RUSSELL, J. S. RISIEN, M.D., F.R.C.P., 44, Wimpole Street, W. (Sec., 1896-1900; C., 1901-1902.)

1899 RUSSELL, J. W., M.D., M.R.C.P., 72, Newhall Street, Birmingham.

1901 SALAMAN, REDCLIFFE N., M.A., M.B., Wentworth House, Mill Hill, N.W.

O.M. SANDERSON, Sir J. BURDON, Bart., M.D., F.R.C.P., F.R.S., Banbury Road, Oxford.

,, SAVAGE, G. H., M.D., F.R.C.P., 3, Henrietta Street, Cavendish Square. (Pres., 1897; V.-P., 1895, C., 1886-90, 1898.)

1888 SAVILL, T. D., M.D., M.R.C.P., 60, Upper Berkeley Street, W.

O.M. SCHAFER, E. A., F.R.S., University of Edinburgh. (Pres., 1893; V.-P., 1892, C., 1886-98.)

1901 SCHORSTEIN, GUSTAVE, M.D., F.R.C.P., 11, Portland Place, W.

O.M. SEMON, Sir FELIX, M.D., F.R.C.P., 39, Wimpole Street, W. (C., 1899-1901.)

1898 SEWARD, WM. JOSEPH, M.B., Colney Hatch Asylum, N.

O.M. SHARKEY, S. J., M.D., F.R.C.P., 22, Harley Street, W. (V.-P., 1902; C., 1899-92.)

,, SHERRINGTON, C. S., M.D., F.R.S., 16, Grove Park, Liverpool. (C., 1892-95.)

1894 SHUTTLEWORTH, GEORGE E., M.D., Ancaster House, Richmond.

1898 SIMPSON, FRANCIS O., L.R.C.P., M.R.C.S., Rainhill Asylum, Liverpool.

1900 SINGER, H. D., M.D., M.R.C.P., St. Thomas's Hospital, S.E.

1895 SMITH, F. J., M.D., F.R.C.P., 138, Harley Street, W.

1887 SMITH, R. PERCY, M.D., F.R.C.P., 36, Queen Anne Street, W. (Editor of "Brain," 1901-1902.)

1895 SPICER, W. T. HOLMES, M.D., F.R.C.S., 5, Wimpole Street, W.

1901 STAFFORD, WILLIAM, M.B., 110, Mansfield Road, Nottingham.

1895 STANSFIELD, THOS. E. K., M.B., London County Asylum, Bexley, Kent.

1895 STANLEY, DOUGLAS, M.D., 19, Easy Row, Birmingham.

1892 STARLING, ERNEST HENRY, M.D., F.R.C.P., F.R.S., 8, Park Square, N.W.

1901 STEELL, GRAHAM, M.D., F.R.C.P., 96, Mosley Street, Manchester.

1897 STEWART, PURVES, M.A., M.D., M.R.C.P., 138, Harley Street, W.

Elected

1897 Stirling, Wm., M.D., D.Sc., Owens College, Manchester.

1894 Stodart-Walker, A., M.B., F.R.C.P.Ed., 30, Walker St., Edinburgh.

1897 Stoddart, Wm. H., M.D., M.R.C.P., Bethlem Royal Hospital, Lambeth, S.E.

1895 Stout, G. F., M.A., 137, Woodstock Road, Oxford.

1887 Suckling, C. W., M.D., M.R.C.P., 103, Newhall Street, Birmingham.

1888 Syers, Henry W., M.D., M.R.C.P., 75, Wimpole Street, W.

1898 Taylor, F. R. P., M.D., Darenth Asylums and Schools, Dartford, Kent.

1891 Taylor, James, M.D., F.R.C.P., 49, Welbeck Street, W. (C., 1900-2.)

1895 Telford-Smith, T., M.A., M.D., Romansleigh, Wimborne, Dorset.

1898 Thomson, H. Campbell, M.D., M.R.C.P., 34, Queen Anne Street, W.

1889 Thorburn, Wm., F.R.C.S., The Limes, Nelson Street, Manchester. (C., 1901-1902.)

1892 Titchener, E. B., B.A., Ph.D., 72, Heustis Street, Ithaca, N.Y.

O.M. Tooth, H. H., M.D., F.R.C.P., 34, Harley Street, W. (Sec., 1891-95; C., 1896-99.)

1892 Trevelyan, E. F., M.D., B.Sc., F.R.C.P., 40, Park Square, Leeds.

,, Tuckey, Charles Lloyd, M.D., 88, Park Street, Grosvenor Square, W.

,, Tuke, Sir J. Batty, M.D., F.R.C.P.Ed., 20, Charlotte Sq., Edinburgh.

1891 Tuke, Thomas Seymour, M.B., Chiswick House, Chiswick.

,, Turner, William Aldren, M.D., F.R.C.P., 13, Queen Anne Street, W.

1898 Turney, Horace G., M.D., F.R.C.P., 68, Portland Place, W.

O.M. Tweedy, John, F.R.C.S., 100, Harley Street, W.

1901 Vincent, Swale, M.B., 137, Richmond Road, Cardiff.

1888 Voorthus, J. A., M.D., Apeldoorn, 542, Loulaan, Netherlands.

O.M. Waller, Augustus, M.D., F.R.S., 16, Grove End Road, N.W. (Pres., 1900; V.-P., 1899; C., 1894-97, 1901.)

,, Ward, J., D.Sc., Trinity College, Cambridge.

,, Warner, Francis, M.D., F.R.C.P., 5, Prince of Wales Terrace, Kensington Palace, W.

1901 Warrington, W. B., M.D., M.R.C.P., 69, Rodney Street, Liverp

1892 Washbourn, J. W., M.D., F.R.C.P., 6, Cavendish Place, W.

O.M. Watteville, A. de, M.A., M.B., B.Sc., 30, Welbeck (C., 1890-95, 1896-1902; Sec., 1886-89; Editor of " 1900.)

1897 Weber, F. Parkes, M.D., F.R.C.P., 19, Harley St

,, West, Samuel, M.D., F.R.C.P., 15, Wimpole St

1897 White, Ernest W., M.B., M.R.C.P., City of Lo

O.M. White, W. Hale, M.D., F.R.C.P., 65, Harle

1894 Whiting, Arthur J., M.D., M.R.C.P., 142,

1889 Wiglesworth, Joseph, M.D., F.R.C.P., Lancashire.

Elected

1900 Williams, Leonard, M.D., 8, York Street, Portman Square, W.

1894 Williamson, Richard T., M.D., F.R.C.P., 294, Oxford Road, Manchester.

1896 Wilson, Albert, M D., M.R.C.P , Minto House, South Woodford, Essex.

,, Wood, Guy M., M.B., M R C.P , 6, Woburn Square, W.C.

1889 Wood, T. Outterson, M.D., M.R.C.P., 40, Margaret Street, Cavendish Square, W.

1892 Woodhead, G. Sims, M.D., F.R.C.P.Ed., 6, Scrope Terrace, Cambridge.

1899 Wright, Hamilton, M.D., Pathological Institute, Selangor Straits Settlement.

1898 Young, Robert Arthur, M.D., B.Sc., M.R.C.P , 41, Wimpole St., W